Entered as second-class matter at the Post Office at Easton, Pa., under the Act of March 3, 1879.

AMERICAN JOURNAL OF PHARMACY

PUBLISHED MONTHLY BY THE
PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE
A RECORD OF THE PROGRESS OF PHARMACY
AND THE ALLIED SCIENCES

VOL. 92 — NOVEMBER, 1920 — NO. 11

CONTENTS

Price, $3.00 per Annum, in advance. Issued Monthly. Single Numbers, 30 Cents. Back Numbers, 50 Cents.

Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917. Authorized March 13, 1920.

Published at 207 Church Street, Easton, Pa.

Address all communications
For the Editor: To American Journal of Pharmacy, 145 North Tenth Street, Philadelphia, Pa.
For the Business Manager: To H. J. LaWall, Business Mgr., 145 North Tenth Street, Philadelphia, Pa.

THE AMERICAN
JOURNAL OF PHARMACY

NOVEMBER, 1920

EDITORIAL.

TO WORK FOR ONE'S PROFESSION, A DUTY.

With the expulsion of our first parents from the Garden of Eden, came the command: "In the sweat of thy face shalt thou eat bread, till thou return unto the ground." So it was ordained as a perpetual law of the Omniscient that man, the highest of all created beings, must be sustained throughout his existence by his own labor. Despite the ages that have passed since the promulgation of this Divine edict, man, as yet, has formed but an imperfect conception of the creation known as *man* and of the perfection of this mechanism and the possibilities of the mental activity and physical energy stored within the human frame.

Labor applied in accordance with the Creator's injunction "to till," "to produce," and with the energy that will cause the worker to sweat, is the foundation of all achievement and the source of true happiness. He who fails in the application necessarily also fails to get out of his work any real satisfaction or enjoyment and will never know what true happiness is. Application of the God-given talents is "the thing that counts."

"Not what we have, but what we use;
Not what we see, but what we choose—
These are the things that mar or bless
The sum of human happiness."

If one studies only the limited circle with which he is brought in contact in his daily routine, he will perceive a variety of characters and a diversity of actuating motives and, moreover, will obtain a new view of the proverbial perversity of the human nature. Doubtless, he will note the very large percentage of those that he meets who are engaged in the purely selfish chase after wealth. In this scramble after dollars, they appear indifferent to the higher ideals

of manhood and the obligations of true citizenship. A real estate dealer recently stated to the writer that his "aim was to get a big pile and to get it quick!" His sentiments and manner suggested that he might become a safe companion for a safe cracker. Then there is the type whose sole ambition is the seeking of notoriety and by one means or another these manage to keep continually in the lime light of public notice. Then there is that other large group composed of the shirkers and slackers who are forever playing the "let George do it" act. The world is to-day, possibly more than at any other period, cursed with these drones and buzzards whose failure to labor and produce constitutes a most serious world-wide problem. Less conversation and more perspiration is the lesson that is needed. Likewise, the misfits are in evidence; those who, after a fashion, are applying themselves to jobs unsuited to their mental or physical abilities and the enormous loss resulting thereby is another problem that society must sooner or later rectify. Our picture presents other heterogeneous types which we can leave to the imagination of the reader.

Nevertheless, despite this picture of the social condition, we are optimistic and believe that the world is slowly, yet surely. getting better and that fortunately there is an ever increasing proportion of its inhabitants who realize that within their respective spheres of labor they have a responsibility to society and are endeavoring to faithfully discharge same. The vocation is immaterial to this contention. Be it that of the professional man, banker, merchant, manufacturer, farmer, mechanic or day laborer, each has his share in the responsibility and his productive labor is but the service that he owes to society and is his expected contribution to the progress of the world. Work brings its own reward with advancement to the individual and enrichment of his country.

We would draw a sharp distinction between that service to society which is presumed to be rendered by every one and the duty which a member of a profession owes to that profession. The man or woman who enters upon a professional career should be imbued with the true professional spirit and, with a sense of the seriousness of the life's work, give thoughtful consideration to the obligations assumed in the practice selected. There is much more in a professional career than anticipated financial recompense and the pride of social position accorded thereto. Self gratification accomplishes nothing for the profession or of permanent benefit to the individual. The

ideals of the professions are upon a more ethical plane that does not contemplate such shallowness and selfishness. Unquestionably, there is need that these be maintained by a more exacting practice.

No person has rightfully a place in a profession that he does not love. The mere fact that he has succeeded in passing the required examinations for the diploma and the license to practice does not signify that he is enthused with the spirit and love of the profession and that its ideals can be safely entrusted to his care. It is far more essential that he possess that love for the sciences and associated labor of his profession that will impell him to assume his full duty as a faithful contributor toward scientific progress and the continued advancement of his profession. To Theodore Roosevelt is credited the pertinent statement that "every man owes some of his time to the upbuilding of the profession to which he belongs."

Altruism should be the guiding principle of the professions. We cannot selfishly live for self alone. We share in the enjoyments, pleasures and benefits resulting from others labors and so it becomes us likewise to contribute our full quota to the sum of human knowledge, public welfare and the world's progress. Especially is it incumbent upon the members of a profession that the duty to one's profession is discharged in accordance with opportunity and in the true ethical spirit. The following short poem beautifully presents the thought of the mutual enjoyment of the benefits of labor.

MY NEIGHBOR'S ROSE.

The roses red upon my neighbor's vine
Are owned by him, but they are also mine,
His was the cost, and his the labor, too,
But mine as well as his the joy, their lovliness to view.

They bloom for me, and are for me as fair
As for the man who gives them all his care.
Thus I am rich, because a good man grew
A rose-clad vine for all his neighbor's view.

I know from this that others plant for me,
And what they own, my joy may also be,
So why be selfish, when so much that's fine
Is grown for you, upon your neighbor's vine?—*Gruber.*

THE THEORY OF PERCOLATION.

By James F. Couch.

WASHINGTON, D. C.

The process of percolation stands at the very foundation of the art of Pharmacy for it represents the first operation in the preparation of a plant drug for medicinal use. The list of organic products is small whose manufacture does not involve percolation at some stage, usually the primary process, and so most of our drug compounds bear witness to the importance of this process. The percolator is a truer sign of pharmacy than the gilded mortar and pestle which so long directed the wayfarer to the apothecary shop, for the mortar suggests little more than the grinding together of the bitter ingredients of some heroic mixture or the powdering of some exotic and expensive root.

In the percolator, however, we can visualize the pharmacist's conquest of the crude materia medica; his ability to select and reject among the constituents of leaves and barks; the softening of the rigors of medication; development of certainty in dosage; and elimination of inert and deleterious matters from pharmaceuticals. Without percolation we should lose a valuable means toward the attainment of these ends.

From the very importance of the process we should expect that pharmacists should give it much attention and be fully informed on the various phases it presents; we find, however, a general neglect, particularly in recent years, of the whole subject. Indeed, it has too many times happened that pharmaceutical assemblies have been bored with discussions which attempted to penetrate farther into the mists which obscure our knowledge of the process. We find not only neglect, but in many cases, a lamentable ignorance of some of the first principles of percolation. We see gross lack of judgment in the choice of menstrua; carelessness in the details of packing the drug, of maceration, or of rate of percolation, and frequently no discrimination in the handling of drugs of widely different character. The work of extraction in pharmaceutical factories is too often left to men of small education who have but the slightest knowledge of the drugs they are extracting, whose ideas of the process are sometimes absurd, frequently extravagant, and generally erroneous, who do not appreciate the delicacy of the whole operation and are, therefore, crude

in manipulation and careless in detail. Nor is this lack of proper appreciation of the principles which underlie the process confined to such men; one questions the average pharmaceutical graduate in vain along lines which demand a broad, general survey of the subject.

The result of such conditions appears at once in the products. An examination of fluidextracts of different manufacture will reveal astonishing diversities in products made from the same drug and, presumably, by the same process.[1] Even in the case of the assayed preparations, the standard quantity of alkaloid or other active component is usually the only point of agreement.

It has, therefore, appeared desirable to survey our whole published knowledge of the process of percolation, widely scattered as it is throughout the literature and much of it inaccessible to the average worker; to examine it critically, state what facts appear definite, and particularly to direct attention to those questions which have not been investigated or which have been left in such an indefinite condition that further research is necesssary to answer them.

HISTORICAL DATA.

The beginnings of percolation as a pharmaceutical process have been traced in an earlier memoir[2] and do not need extended description in this place. It is there shown that the credit for the establishment of the process of percolation in pharmacy is due to the Boullays of Paris, who, in 1833, published their work on the process of displacement,[3] and detailed discussion of the previous work of Real, Cadet, Robiquet and others is included. The earliest American notice of the process is the quotation of M. Soubeiran's memoir on "displacement" in this Journal.[4] Augustine Duhammel,[5] was the first American to publish any account of an original examination of the process. He states that the process had been in extensive use in Germany, "and elsewhere" for twenty years and that E. Durand was the first to use

[1] Haussmann, *Proc. A. Ph. A.* 1895, 564; Lloyd, This Journal, Vol. 80, p. 39; A. Conrath, *Proc. A. Ph. A.* 1882, 545; Spenzle, *Proc. A. Ph. A.* 1882, 547; *Linde Ph. Centr.* 1894, 39; This Journal, Vol. 66, p. 141; C. L. Diehl, *Proc. A. Ph. A.* 1878, 681.

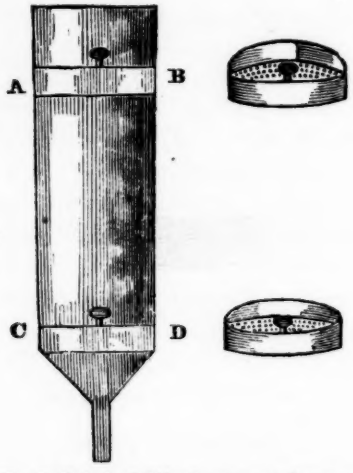
[2] This Journal, Vol. 91, 16, (1919).

[3] *Jour. de. Pharm.* 19, 2281, (1833); 19, 393, (1833).

[4] This Journal, Vol. 8, 221, (1836).

[5] "Boullay's Filter and System of Displacement with Observations Drawn from Experience." This Journal, Vol. 10, 1, (1838).

the process practically in this country. This memoir was followed a year later by "Observations on the Method of Displacement" by Augustine Duhammel and William Procter, Jr.[1] in which the advantages of the new process are clearly stated and its adoption is recommended.



Boullay's Original Displacement Apparatus

At C-D was placed a metallic diaphragm pierced with holes and provided with a handle and fitting accurately, designed to prevent the escape of the drug. At A-B a similar sieve was placed, intended to hold down the drug and scatter the liquid over the surface.

Percolation was then made official in two pharmacopoeias, the Edinboro pharmacopoeia of 1838 and the U. S. P. of 1840, published in 1842.[2]

Percolation quickly became a popular process in the United States; it does not appear to have attracted as much attention in any other country if we can be guided in judgment by the absence of more than scattering comments upon it in the foreign journals. American pharmacists, however, quickly perceived its advantages and began to study and apply the process. In 1847, E. T. Ellis[3] and Wm. Procter, Jr.[4] published formulas for the fluidextracts of Valerian, and Rhubarb and Valerian, respectively, and these papers were followed by published formulas for various other fluidextracts by Proc-

[1] This Journal, Vol. 11, 189, (1839).
[2] This Journal, Vol. 14, 125, (1842).
[3] This Journal, Vol. 19, 83, (1847).
[4] This Journal, Vol. 19, 182, (1847).

ter, Savary, Taylor, and others which gave evidence of intelligent comprehension of the principles involved in percolation and careful study of the drug and the menstrua suitable for its extraction.

The critical study of the process of percolation began in 1858 with Squibb's first paper,[1] although one critical commentary, that of Deane,[2] had already been published. For the next twenty-five years Squibb frequently contributed critical essays on percolation to the periodical literature. Procter, Maisch, Diehl,[3] Redwood,[4] Signoret,[5] Parrish,[6] Graham,[7] A. B. Taylor[8], McIntyre,[9] Remington[10], Moore,[11] Robbins,[12] and J. U. Lloyd supplemented and extended the work of Squibb. Lloyd appears first in 1877[13] and within a few years was easily the leader in this field of investigation. He has devoted much of his time during the past forty years to a study of percolation and the conditions affecting the process and its products. We owe by far the larger proportion of our knowledge of extraction to his patient industry and unselfishness.

Early in the Sixties, Squibb interested himself in the question of economy of alcohol in percolation[14] following the increased price of that solvent due to federal taxation. This study led to the development of his famous "repercolation" process[15] and led to a controversy that stimulated investigation and developed page after page of most valuable observations and deductions. The process of Squibb was not made official in the U. S. P. until the ninth revision (1916) although permission to use it was given in earlier revisions. It was considered that the complicated manipulations of Squibb's method were not suited for general pharmaceutical use[16] although it was admittedly an improvement.

[1] This Journal, Vol. 30, 97, (1858).
[2] *Pharm. Jour.* Vol. 1, 61, (1841).
[3] This Journal, Vol. 41, 337, (1869).
[4] *Pharm. Jour.* Vol. 23, 523, (1864).
[5] This Journal, Vol. 33, 319, (1861); from *Répertoire de Pharm.*
[6] This Journal, Vol. 31, 327, (1859).
[7] This Journal, Vol. 31, 354, (1859).
[8] This Journal, Vol. 42, 150, (1870).
[9] This Journal, Vol. 45, 210, (1873).
[10] This Journal, Vol. 46, 7, (1874).
[11] This Journal, Vol. 46, 497, 551, (1874).
[12] This Journal, Vol. 50, 329, (1878).
[13] *Proc. A. Ph. A.* 1877, 408.
[14] *Proc. A. Ph. A.* 1865, 201; This Journal, Vol. 38, 109, (1866).
[15] *Proc. A. Ph. A.* 1867, 391.
[16] This Journal, Vol. 41, 295, (1869).

Since the Seventies, a large number of memoirs bearing directly on the problems of percolation has been published and, of these, the larger proportion has resulted from the work of American pharmacists. The behaviors of different drugs in percolation have been compared, the effects of altered conditions studied, the factors which govern the permanence of the products investigated, new menstrua experimented with, much analytical data accumulated, and a host of new apparatus and methods developed and proposed. All of this work shall be considered in detail in the course of this survey and with this, we terminate the brief historical sketch, which to develop more fully would carry us into discussions which properly belong under other headings.

DEFINITIONS.

The term percolation, as generally used in this country, may be defined: a continuous process for the selective extraction, by a suitable solvent or mixture of solvents, of the soluble constituents of a mixture of substances part of which are insoluble in the solvent selected, conducted in such a way that the solvent travels through the mass to be extracted, from one surface of which the partially saturated solution is removed while fresh solvent is admitted at the opposite surface. The process is carried out in an apparatus called a percolator, of various designs and made of various materials for special purposes, usually of glass, shaped like a frustrated cone with the smaller end sharply constricted to a small tubular opening which may be fitted with a stopcock. In pharmaceutical practise the material percolated is usually called a drug and the solvent used is termed the menstruum. The solution as it runs from the percolator is known as the percolate, its dissolved matter is termed the extract, and the exhausted drug which remains in the percolator at the conclusion of the process is called the marc. The soluble constituents of the drug before their appearance in the percolate are included in the term extractive. It appears desirable, for theoretical reasons, to make a distinction between the undissolved soluble material and that actually in solution. Moreover, as there is frequently a chemical difference between the solution within the percolator and in contact with the drug, and the percolate, which is no longer in contact with the drug, it would seem advisable to distinguish between them by a specific name for the former. In this survey the term *precolate* will be used to specify the liquid found between the initial and terminal surfaces of the drug and in contact with it.

THE PERCOLATOR.

The design of the apparatus in which percolation is to be conducted has received a great deal of intelligent attention and in this narrow field, our knowledge may be regarded as very nearly complete. Nearly every thoughtful pharmacist has studied the subject and the result is that scores of new percolators have been suggested during the past eighty years. Many of these have involved innovations or radical changes in the process of extraction and are thus more related to some specific method than to general percolation. For this reason those percolators which substitute apparatus without affecting the process seriously will alone be considered in this section; the others will be analyzed when we discuss the unusual and special methods of percolation.

The early apparatus of the Boullays was essentially the cylindrical percolator sometimes seen to-day. Emil Mouchon of Lyons[1] substituted a funnel and the concial shape is first recorded in Gilbertson's apparatus.[2] The very tall, nearly cylindrical percolator was advocated by Oscar Oldberg in 1884.[3] The funnel shaped, the conical, and Oldberg's percolators are in common use to-day, the conical being the form most widely used. The essential difference between the three forms is, of course, the taper upon which depends the height of the column of drug and the number of contacts between each particle of drug and each aggregate of menstruum as well as the relative number of such contacts for the drug in the widest part and that in the narrowest part of the percolator.

Lloyd has shown[4] that the longer the column of drug is, the more concentrated the first portions of percolate are and he states two rules: first, that the height of both liquid and powder increase inversely as the square of the diameter of the percolator, and second, the contact between the liquid and powder increases inversely as the fourth power of the diameter of the percolator. The efficiency of the Oldberg design has also been confirmed by E. Moor, Jr.[5]

The importance of securing as much concentration in the early portions of the percolate as possible, other things being equal, is obvious. Nevertheless, for operations involving large amounts of

[1] Squibb, *Proc. A. Ph. A.* 1867, 391.
[2] *Pharm. Jour.* 1, 591, (1842).
[3] *Proc. A. Ph. A.* 1884, 388.
[4] *Proc. A. Ph. A.* 1879, 679.
[5] This Journal, Vol. 62, 333, (1890).

drug, as in the manufacture of several gallons of a fluidextract, the difficulty in unpacking a narrow, slightly tapering percolator is so great that the conical shape is used almost exclusively in such operations although its diameter is very much larger in proportion to its capacity. For such purposes a percolator as designed by A. B. Taylor[1] where the length is twice the largest and four times the smallest diameter will serve excellently.

The use of the funnel shaped percolator has provoked much discussion. The diameter of the percolator changes so greatly from the bottom upwards that the topmost layers of drug, which receive the fresh menstruum, are in contact with a much smaller amount per unit weight than the lower layers. The lower layers are acted upon by the most saturated menstruum the solvent powers of which are less than those of the fresh menstruum and, in the funnel percolator, the effect of the narrowing diameter is to force this partly saturated menstruum into longer contact with the drug than is the case higher up. The result is that, as the menstruum becomes laden with extractive and consequently weaker in solvent powers, it is forced to lie in contact with unit weight of drug for a longer time and this effect is distributed throughout the percolator in proportion to the diameter. The great advantage of the funnel percolator has been considered to be the fact that its taper will permit a drug which swells much during percolation to push its way upward instead of packing very firmly in the percolator as will happen in percolators of slight taper.

Campbell used the funnel percolator in his method for the preparation of fluidextracts without heat[2] which was approved by A. B. Taylor[3] and Kennedy,[4] although Reynolds,[5] King,[6] and Archibald[7] were unable to exhaust the drug thoroughly with the small quantity of menstruum permitted by Campbell's process. Taylor's experiments showed, however, that a very concentrated first percolate could be obtained with a funnel percolator if four days were allowed for the preliminary maceration. The use of this type of apparatus

[1] *Proc. A. Ph. A.* 1869, 390.
[2] This Journal, Vol. 41, 384, (1869); Vol. 42, 17, (1870).
[3] *Proc. A. Ph. A.* 1869, 390. This Journal, Vol. 42, 150, (1870).
[4] This Journal, Vol. 42, 62, (1870).
[5] This Journal, Vol. 41, 525, (1869).
[6] This Journal, Vol. 42, 29, (1870).
[7] This Journal, Vol. 42, 117, (1870).

was also advocated by Graham[1] and Cohen.[2] Squibb,[3] Parrish,[4] Lloyd,[5] and Remington,[6] have considered the more cylindrical shapes superior to the funnel and have discountenanced the use of the latter except for dilute preparations such as tinctures and wines.

There is one factor in this connection which has not been investigated and, indeed, which has too often been neglected in studies on extraction. That is the time factor. It is obvious that a given volume of menstruum will pass through a drug packed in a funnel much more rapidly than it will pass through the same amount of drug packed in a long, narrow percolator. Under such conditions we cannot expect the percolate from the funnel to contain as large a proportion of dissolved matter as that from the less tapered vessel, but we do not know what the relation between equal quantities of percolate from the two or three forms would be if the flow from the funnel were retarded to the same rate as that from the other apparatus, both delivering the same volume of percolate in the same time. Inasmuch as, within certain limits, the concentration of the first portions of percolate depend upon the length of time the menstruum has been in contact with the drug, the time factor is of great importance in comparing such percolators as these and, on account of the neglect of it, the whole subject demands further investigation.

In the hands of the inexpert or the careless operator the Oldberg or nearly cylindrical percolator will doubtless give more uniform results and a more concentrated first percolate such as is used for the reserved portion in the manufacture of fluidextracts. The conical form will prove nearly as efficient and has the advantage of being more easily unpacked.

Modifications of these three shapes have been introduced from time to time to adapt them to special purposes. Many forms of closed percolators have been described for use with volatile solvents such as ether, chloroform, benzine, or acetone, designed especially to minimize loss of the solvent through evaporation. Gilbertson's apparatus[7] was one of the first of these and it is very compact and

[1] This Journal, Vol. 31, 354, (1859).
[2] This Journal, Vol. 44, 8, (1872).
[3] This Journal, Vol. 38, 109, (1866).
[4] This Journal, Vol. 31, 327, (1859).
[5] *Proc. A. Ph. A.* 1877, 405.
[6] *Drug. Circ.* 1884, 148.
[7] *Pharm. Jour.* 1, 591, (1842).

ingenious. Arny has also devoted his attention to this subject and has proposed several practical and serviceable forms,[1] in which the menstruum is kept out of contact with the air. That it is not necessary to have a tubular percolator in which menstruum enters at one end and percolate issues at the opposite end was shown by Squibb[2] with his tub percolator. Several other ideas[3] in percolator design were worked out by this indefatigable pharmacist and are worthy of the attention of every worker in the field of extraction.

Finally, a word may be said about the materials of which a percolator is constructed. Glass is the best material at hand and practically all small percolators are made of it. It possesses many advantages; transparency, so that the process may be closely watched and inequalities of flow, due to improper packing or accident detected, cleanliness; and minimum solubility, so that foreign matter is kept out of the product and undesirable reactions with the drug avoided. Its fragility, however, makes it impractical for apparatus larger than three or four gallon capacity unless it is reinforced as in the glass lined percolators of wood or metal. Lloyd's experience with glass percolators of ten gallon capacity confirms this statement.[4]

Large size percolators are commonly made of galvanized iron, some are made of tinned copper or iron, and some of stoneware. The galvanized iron percolator is strong, substantial, and inexpensive. It resists the corroding action of acid plant solutions very well but contaminates the percolate with small, nearly negligible amounts of zinc and iron. It is somewhat difficult to clean thoroughly and sooner or later rusts through and becomes unserviceable. Tinned iron percolators offer no advantage and rust through more quickly than the galvanized iron percolators. Iron percolators with enamelled inside surface are extensively used and are serviceable for most drugs. Tinned copper percolators are expensive and cumbrous and contaminate the percolate with small quantities of tin. Percolators of stone or earthen ware are frequently used for large batches of drugs which are to be extracted by strongly acid menstrua which would rapidly destroy metallic apparatus. A five or ten gallon stoneware jug from which the bottom has been removed makes a very useful percolator of this type. Plain wooden percolators are seldom used. They are

[1] *Proc. A. Ph. A.* 1892, 169.
[2] *Proc. A. Ph. A.* 1872, 182.
[3] *Proc. A. Ph. A.* 1878, 708.
[4] *West. Drugg.* 11, 159, (1888).

uncleanly, heavy, and not strong enough to withstand the great pressure developed by a swelling drug unless reinforced by many iron hoops.

THE DRUG AND ITS PREPARATION FOR PERCOLATION.

Plant drugs may be classified in a variety of ways but, for our purposes, their behavior toward solvents is the criterion of their relationships. From this point of view we may propose the following classification. I. Resinous drugs, cimicifuga, cannabis, balm of gilead, whose active principles are usually extracted only by strong alcohol. II. Terpene drugs, peppermint, buchu, thyme, whose active principle is a terpene or a terpene derivative demanding a menstruum rich in alcohol. III. Alkaloidal drugs, gelsemium, nuxvomica, belladonna; the menstruum depends upon the individual solubility of the alkaloid and the condition in which it exists in the plant. In general strong alcohol is needed for those plants which contain free alkaloids; dilute alcohhol is employed where the alkaloid exists as a salt. Acid menstrua are often employed in the extraction of this class of drugs, *e.g.*, ergot, lobelia, sanguinaria. IV. Glucosidal drugs. The solubilities of the glucosides vary widely from insolubility to free solubility in water and dilute alcohol. Menstrua employed for this class vary from water in the case of cascara to alcohol for strophanthus. The majority of them may, however, be extracted with dilute alcohol. V. Oleoresinous drugs. Pepper, parsley, aspidium. These drugs are extracted with ether or the less expensive acetone, for the loss of solvent through evaporation may be quite large in spite of precautions. VI. Tannin-containing drugs. Kino, rubus, krameria. These drugs are extractible with water. However, aqueous solutions of their extracts are apt to gelatinize so the drugs are extracted with menstrua containing alcohol and glycerin is added to the first portions of percolate. Sometimes glycerin is used in the menstruum. VII. Saponin drugs, quillaja, sarsaparilla, squills, senega. The saponins are soluble in water and insoluble in cold alcohol. The menstruum usually used is diluted alcohol, the alcohol being employed as a preservative. Diluted acetic acid is of course, a favorite menstruum for squills. VIII. Mucilaginous drugs. A. Elm, chondrus; B. senna, uva ursi. These drugs are extracted in two ways according whether the mucilage is desired or not. A. Where the mucilaginous substance is to be extracted the drug is treated with hot water but is not usually percolated. B. If the mucilage is undesirable in the

product the drug is extracted with an alcoholic menstruum in which the mucilage is insoluble. In such cases the drug may be placed in another classification, senna in class IV and uva ursi in class II. IX. Acid drugs. Licorice, triticum, zea mays, mostly extractible with water, more easily with alkaline menstrua. Licorice is extracted with dilute ammonia. Rhubarb may be extracted with water but its content of mucilage presents practical difficulties so that dilute alcohol is usually employed. X. Miscellaneous drugs, requiring special treatment on account of individual peculiarities, prunus virgiana, gentian, quassia.

The class to which a drug is to be referred, then, will depend upon the nature and solubility of its active principle modified by the solubilities of undesirable ingredients which the plant may contain or by the exigencies of preserving the product. This classification is thus strictly pharmaceutical and very different from botanical or therapeutical systems. Drugs exhibit, however, such individualities that it is difficult to draw many generalizations about them.

This point is particularly true in the preparation of drugs for percolation. Squibb remarked[1] that the process of percolation differs materially with every drug and every menstruum used. The master of percolation varies the details of his process from beginning to end to suit the characteristics of the drug.

The extraction of a drug properly begins with the grinding of the crude material, proceeds through its moistening, maceration, packing and the actual percolation to the emptying of the exhausted marc into the dreg still. As all these steps are of considerable importance the following pages will bear a detailed discussion of each in order.

The fineness of the drug, that is the degree of comminution or the size of its particles, is a factor upon which depends, in no small measure, the success of percolation. Little has been published on this subject and that has been largely opinion based on practical experience and not upon critical experiment. The general agreement is that the finer the drug powder, the more efficient the extraction and the pharmacopoeia revels in number sixty powders. Squibb[2] thought a number 24 powder fine enough and Procter[3] allowed as coarse powder as Nos. 25 to 30 for mucilaginous drugs but preferred a fine

[1] *Proc. A. Ph. A.* 1869, 305.
[2] This Journal, Vol. 30, 97, (1858).
[3] This Journal, Vol. 31, 317, (1859).

powder.[1] Campbell[2] recommends a No. 40 powder. Lloyd[3] showed mathematically the probability of greater efficiency in extraction the finer the drug powder and Rosenwasser[4] developed the same conclusion. The following figures[5] for the yield of extract by

Menstruum.	Coarse Powder.	Fine Powder.
Cold water	32.94–39.82 per cent.	35.25–35.42 per cent.
Boiling water	40.19–41.22 "	38.68–38.91 "
Dilute alcohol	38.57–41.3 "	40.3 "
68 per cent. al.	36.32–39.31 "	39.1 "

maceration of gentian of different fineness and with various menstrua show a difference: Feil[6] reported 31.5 per cent. extract from gentian by percolation. The figures in the above table show more uniform results in extract yield from the finely powdered drug yet with every menstruum the coarse drug yielded more extract than the fine which is quite contrary to expectation.

In considering the differences in different degrees of fineness the time factor has again always been neglected. Any menstruum will pass more quickly through a coarse drug than through one that is finely powdered and is, therefore, in contact with the drug and able to exert its solvent action for a much shorter period of time. In my own experience I have known two weeks to elapse after flooding a percolator which contained 83 pounds of gentian in No. 60 powder before the percolate appeared. There is need of some careful investigation to furnish data in which all the factors are included. The results quoted above were obtained by maceration so that the time-contact factor is eliminated from the figures and they show a slight favor towards the coarse drug. If this time-contact factor were eliminated in percolating powders of the same drug of different degrees of fineness, by commencing the percolations after the same elapse of time after packing and adjusting the rate of flow of percolate to the same volume per hour for all cases the results furnished would contain no interfering factor and such data would serve as a basis for really valuable conclusions upon the relative merits of different degrees of fineness.

[1] This Journal, Vol. 36, 1, (1864).
[2] This Journal, Vol. 41, 384, (1869).
[3] *Proc. A. Ph. A.* 1879, 682.
[4] *Proc. A. Ph. A.* 1882, 519.
[5] *Proc. A. Ph. A.* 1906, 746.
[6] *Proc. A. Ph. A.* 1906, 433.

The general manufacturing practise at present is to use drugs ground to about a No. 12 powder. This is much coarser than the pharmacopoeia recognizes but is justified by the magnitude of the operations. There is present in such a drug powders of all degrees of fineness up to impalpability and this lack of uniformity is undesirable but unavoidable.

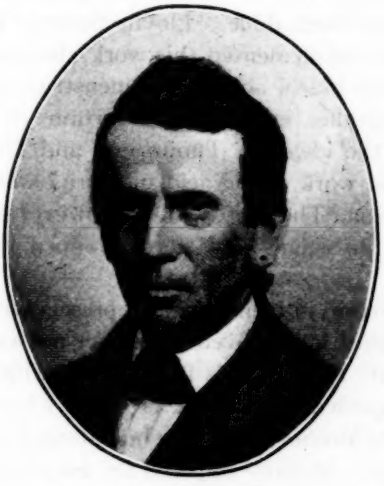
There is, too, a practical limit to the fineness of a powder which can be extracted with diluted alcohol. Consider a mucilaginous drug such as senna, gentian, uva ursi, or buchu, and in No. 60 powder. As the precolate descends through the drug it dissolves the extractive and also the drug moisture, an important constituent for practical reasons. This means that the alcoholic strength of the precolate is constantly diminishing and, if the column of drug be long enough, a point will be reached where its alcoholic strength is so low that the mucilage will begin to swell, preparing to dissolve, and, covering every particle of drug with a continuous slimy film, will clog the percolator, oppose the passage of the precolate, and probably terminate the process. In such a case one of two expedients must be resorted to in avoiding such an exigency; either the drug must be coarse enough to permit the passage of the precolate before it has become so dilute in alcoholic strength, or these large lots of very fine drugs must be extracted with menstrua of high alcoholic content. The variation of the menstruum is, in most cases, permissible only within very narrow limits and so the operator is forced to use coarser drugs for large batches. With pharmacopoeial quantities of 1,000 grams such factors do not enter into consideration, and it is possible that there exists a rational relationship between the quantity of drug to be extracted and the fineness required. Perhaps a No. 20 powder is to a No. 60 as a five litre product is to a one litre.

Another factor which must be considered is adsorption. How important this phenomenon is will be discussed later but in this connection it should be noted that adsorption resists extraction. It is an opposing force, and, being a surface phenomenon, increases with the enlargement of the drug surface, that is with increasing fineness of drug. It is known that in many cases the amount of substance adsorbed is less in alcoholic liquids than in aqueous solutions and the factor may disappear in strongly alcoholic percolates. Lloyd has established the fact of adsorption in pharmaceutical processes[1] and the literature on the physicochemical aspects of the phenomenon is

[1] *Proc. A. Ph. A.* 1885, 411.

voluminous, but much remains to be done before its rôle in percolation is made clear.

We cannot, therefore, conclude in favor of any one general optimum fineness for a drug. We may say that, the stronger the menstruum to be used is in alcohol the finer the drug may be powdered and as strongly alcoholic menstrua tend to shrink, instead of swelling, vegetable fibres and cells, the finer the drug the better in such cases. In general, the drug should be ground to as fine a powder as will be permitted by its character, the menstruum, the quantity being extracted, and the time available.



PROF. WILLIAM PROCTER, JR.

A pioneer advocate of the pharmaceutical application of percolation.

When the drug has been ground to the desirable fineness the next step in the process is the moistening of it and this brings up the selection of the menstruum. Here we find that a multitude of pharmacists have done very good and careful work for it was early recognized that not only the proper extraction but the permanence of the product depends upon the suitability of the menstruum. In choosing a menstruum the principles enunciated in the discussion of the classification of drugs must be borne in mind as well as the idea of the ideal menstruum which is such a one that will perfectly dissolve the active constituents and exclude undesirable ingredients furnishing a product that may be readily preserved.

The situation in respect to menstruum is excellent mainly because they have been chosen as a result of many experiments the conditions of which point definitely and unmistakably to the correct choice. Menstrua are usually chosen much in advance of any very detailed analysis of the drug plant and knowledge of the chemical and physical nature of the active constituents. Indeed, our lack of knowledge in this respect has been responsible for much empiricism in the application of menstrua. We have, however, succeeded in establishing a proper solvent for every important drug, though in most cases our products are not free from precipitation.

We are indebted to Procter[1] for initiating and prosecuting much of the work which has been done. Lloyd,[2] Savery,[3] Remington,[4] and a host of others have supplemented this work. Remington[5] and Squibb[6] have advocated the use of acetic acid menstrua, proposing to eliminate alcohol altogether in extracting certain drugs. Wulling[7] and Feil[12] supported the idea but Thompson[9] and Dohme[14] opposed it. As a result of thsi work acetic acid menstrua were directed by the 1900 pharmacopoeia. The preparations, however, failed to meet with the approval of physicians and were dropped in the last revision (1910).

The use of glycerin in menstrua as a preservative agent was early suggested by Taylor[8] and proved a distinct advance in fluidextract technique. Lloyd[9] recommends it for drugs which contain tannins and Lehman[10] regarded it valuable for drugs whose active principles are soluble in both alcohol and water but discards it for mucilaginous and resinous drugs. Moore[11] opposed the use of glycerin in menstrua

[1] This Journal, Vol. 19, 182, (1847); 23, 218, (1851); 24, 207, (1852); 26, 28, (1854); 25, 410, (1853); 28, 22, (1856); 31, 530, (1859).

[2] *Pharm. Rund.* 1889, 165.

[3] This Journal, Vol. 23, 119, (1851).

[4] This Journal, Vol. 46, 7, (1874). Cf. Squibb, This Journal, Vol. 39, 289; 398; 513, (1867).

[5] This Journal, Vol. 69, 121, (1897); 70, 543, (1898).

[6] This Journal, Vol. 71, 1, (1899); 72, 1, (1900).

[7] *Pharm. Era*, 1898, 796.

[8] *Proc. A. Ph. A.* 1908, 883.

[9] This Journal, Vol. 71, 67, (1899).

[10] *Proc. A. Ph. A.* 1904, 337.

[11] This Journal, Vol. 37, 50, (1865).

[12] *Proc. A. Ph. A.* 1877, 408.

[13] This Journal, Vol. 49, 346, (1877).

[14] This Journal. Vol. 46, 551, (1874).

unless it is a better solvent than either alcohol or water as it "interferes with percolation."

Beringer[1] has devoted much attention to the use of glycerin as a solvent and preservative. As a result of his work a new class of official preparations, the fluidglycerates, has been introduced. Ripptoe[2] has shown that the fluidglycerates of digitalis and ergot are very much less active physiologically than the corresponding fluid extracts.

When the menstruum has been decided upon the drug is moistened with a portion of it and allowed to stand several hours to swell. This is done for practical reasons, *viz.*, to assist in packing, to allow a modification of the conditions of the drug constituents, and to insure the saturation of every particle of drug with menstruum so that the actual percolation may affect all the drug evenly. Some drugs need not be moistened,[3] as cimicifuga, cubebs and resinous or oleoresinous drugs which are extracted with alcohol, ether, chloroform, or petroleum ether and similar solvents and consequently do not swell in the percolator nor yield a viscous percolate. I believe, however, that it is better to moisten a drug before packing in all cases where it is practically and economically convenient.

A dry drug cannot be packed as evenly nor as firmly as one that has been moistened and, with uneven packing, the operator is doomed to get irregular extraction with probable incomplete exhaustion.

With certain drugs it is often desirable to modify the nature of the conditions in which the constituents exist. Alkaloidal drugs are often extracted with acid menstrua to increase the solubility of the bases and their rates of extraction. At other times it is desired to carry out the percolation in an alkaline medium, or perhaps, an alkaloid which exists as a salt in the plant is to be extracted with a menstruum, like benzol, in which the free alkaloid, but not its salt, is soluble. Or some treatment is required to render insoluble or to destroy an undesirable constituent as in the case of cascara sagrada.

In such cases it is usually best to make the modification at the time the drug is being moistened. Thus the quantity of acid, diluted with a portion of menstruum, is added all at once to the drug and evenly distributed through it. With ergot, lobelia, ipecac, etc., this is a stock method. In making alkaline a drug which is to be

[1] This Journal, Vol. 79, 410, (1907); Vol. 80, 525, (1908); Vol. 81, 475, (1909).
[2] This Journal, Vol. 81, 84, (1909).
[3] This Journal, Vol. 31, 317, (1859).

extracted with a solvent immiscible with water the common practice is to mix thoroughly with a solution of sodium or potassium carbonate, bicarbonate, or hydroxide, or ammonia and dry the mixture. Calcium hydrate, barium hydrate, magnesia or zinc oxide may be similarly handled.

Lloyd[1] has suggested bringing drugs to their natural moisture content by adding water to them and allowing them to swell before treating them with the menstruum designed to extract them. This has not been adopted. Indeed it would necessitate a thorough revision of all our menstrua except those which are strictly aqueous and would give us different products in many cases than those produced by the processes in present use. The resinous and terpene drugs would, of course, be most affected and while it is possible to extract many if not all of these drugs when they are fresh with dilute alcohols, it is doubtful whether the addition of water to the dried specimen, where the plant fluids have lost their solvent, would effect a re-solution of the resinous or terpene derivatives originally held in solution in the plant fluids. Probably the alcoholic menstrua used on such drugs would not dissolve the active principles until the added water had been nearly completely washed out.

An ingenious method of moistening small amounts of drug has been brought forward by Eberle,[2] who places the drug in a covered can, adds the menstruum and stirs. A few glass stoppers are then mixed with the drug and the whole is shaken. The stoppers prevent lumping of the powder and the drug is thoroughly moistened without evaporation of the solvent.

When the drug has been moistened it is customary to allow the mass to remain in a covered container until it has finished swelling. The extent to which drugs will swell as well as the time consumed in the process varies considerably and the variation is due somewhat to the menstrua employed in moistening them. In general drugs will swell more according to the density of their fibre, that is the more compact their cellulose structure is, the presence of mucilaginous or carbohydrate constituents, and the more aqueous the menstruum. The swelling is due to an imbibition of one or more of the constituents of the menstruum and drug particles appear to show much discrimination between the various solvents in use. Water is most readily and most largely absorbed by them, glycerin, acetone, dilute acetic

[1] *Pharm. Rund.* 1889, 165. *Proc. A. Ph. A.* 1890.
[2] *Drug. Circ.* 1900, 11. *Proc. A. Ph. A.* 1900, 398.

acid less, and benzol, alcohol, ether, chloroform, and petroleum ether are still less absorbed. When an hydro-alcoholic menstruum is used it is not uncommon for the drug to absorb more water than alcohol from the menstruum so that the composition of the liquid portion of the drug mass will be different from that of the unabsorbed menstruum, a phenomenon which may have an important effect upon percolation and which, like many others, needs investigation.

When the moistened drug has swollen sufficiently it may be passed through a coarse sieve to break up lumps, though this process is usually omitted, and then packed in the percolator.

The outlet of the percolator is plugged with something to prevent drug from being washed out with the percolate; cotton is used in small operations, excelsior for larger batches. The amount used is so small that the effect on the process due to it, while definite, is negligible. Covering the diaphragm with muslin, cheese cloth, or filter paper is a method quite commonly employed.

The packing of the drug in the percolator demands a certain amount of skill and the personal equation enters largely into it. Individual operators differ widely in the manner in which they pack the drug and it is difficult to devise directions which will lead to the same result in the hands of different men. It is usually stated that the drug should be packed evenly and firmly so as to lead to an even and not too rapid descent of menstruum through it without the formation of channels or regions of varying density in the same horizontal plane. The degree of firmness to be attained depends upon the character of the drug and the menstruum. In general, the looser the drug fibre and the richer the menstruum is in alcohol, the firmer the packing should be. All drugs, however, should be packed very tightly particularly if they have been allowed to swell.

Rosenwasser[1] suggested that greater force should be used in packing the upper layers of drug than was used on the lower layers since the force employed on the upper served also to compress the lower portions and, therefore, if a uniform force were to be used throughout the packing, the lowermost drug would be compressed more than the top layers. This is a valuable practical idea and does not appear to have attracted the attention which it merits.

Another neglected suggestion is that of J. W. Mill[2] who advised the separation of the drug into powders of various degrees of fineness,

[1] *Proc. A. Ph. A.* 1882, 519.

[2] This Journal, Vol. 43, 17, (1871).

moistening and packing separately; packing the finest drug first and the coarsest last so that the fresh menstruum should come into contact with the most difficult drug to extract. This is an early expression of the countercurrent principle now so universally used and the idea is valuable, not only for the above reason, but because a mixture of powders of all degrees of fineness from a No. 12 upwards is very difficult to exhaust satisfactorily.

THE ACTUAL PERCOLATION.

The actual percolation may be considered as beginning with the addition of the menstruum to the packed drug in quantity sufficient

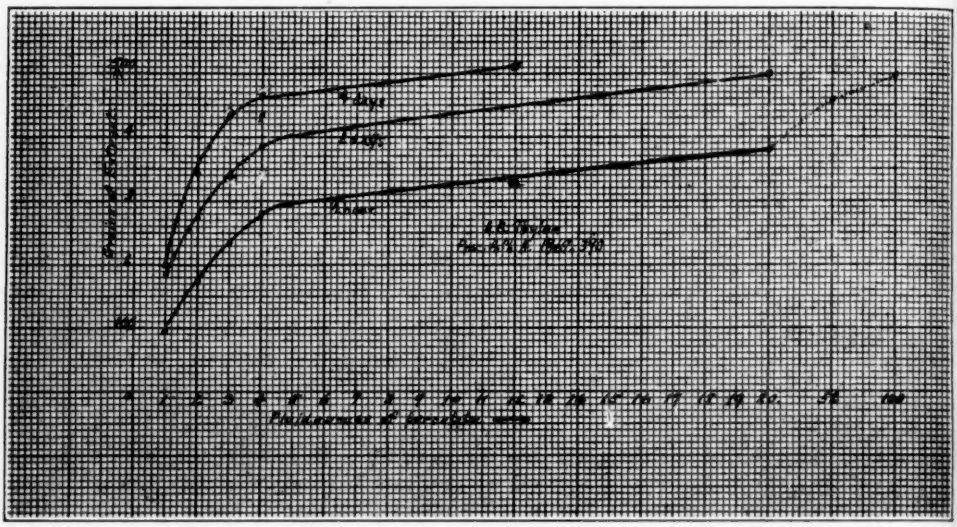


Chart A.

to fill the interstices of the drug and leave a stratum above it. To facilitate the escape of air the stopcock is usually left open until a few drops of percolate issue. The common practise at this point is to shut the stopcock and to leave the whole apparatus at rest for forty eight hours or more. This procedure, termed maceration, has been shown to be very desirable. Procter[1] approved of long maceration and Campbell[2] adopted it as one of the features of his method. Savage[3] showed by experiments with a long list of drugs that long macera-

[1] This Journal, Vol. 36, 1, (1864). *Pharm. Jour.* 19, 139, (1859).
[2] This Journal, Vol. 41, 384, (1869).
[3] *Pharm. Jour.* 24, 254, (1864).

tion produces a much more saturated first percolate. Taylor[1] published figures showing the effect of maceration on yellow cinchona using four troy ounces of drug and a menstruum of diluted alcohol. He macerated individual samples for one-half hour, forty-eight hours, and four days and his results are plotted in Chart. A. This shows clearly the increased concentration due to maceration and the rapidity of exhaustion after it. By two days' maceration he was able to extract as much in 20 fluidounces as were extracted in 100 fl. oz. after the half hour's maceration; and 12 fl. oz. of percolate from the four day experiment contained slightly more extract. Robbins' experiments show the same effect.[2] Edel also advocated lengthy maceration.[3] The following figures were obtained by the writer: the first drippings from the percolator were collected and analyzed, the apparatus was closed and allowed to macerate and the first 100 mils of percolate collected after the maceration was completed. Poke root gave 16.14 Gm. of dry extract per 100 mils of first drippings; after three days' maceration, 18.888 Gm. Passiflora gave 13.636 Gm. of extract per 100 mils of first drippings; after five days' maceration 15.44 Gm.

The optimum length of maceration does not seem to have been investigated. The increase in extract content is not, apparently, proportional to the time of maceration but diminishes as time proceeds. The equilibrium point would probably not be reached for weeks or even months. It becomes, then, a question of judgment to decide when the gain in extract becomes too small to justify the expenditure of time and this must be decided by each operator for himself.

At the end of the period of maceration the stopcock of the percolator is opened and the collection of the percolate begins. At this point we have in the percolator three distinct phases,[4] the partly exhausted drug, the absorbed menstruum, wetting the drug with whatever extractive that menstruum has dissolved, and the precolate or partly saturated menstruum distinct from that which has been absorbed by the drug. Outside the percolator we have a fourth phase, the percolate.

The absorbed menstruum may claim our immediate attention.

[1] *Proc. A. Ph. A.* 1869, 390.

[2] This Journal, Vol. 50, 329, (1878).

[3] *West. Drug.* 1893, 218.

[4] This term is not used in the physico-chemical sense.

A number of questions arise concerning it. Is it displaced by fresh menstruum? Is it constant or variable? Does it differ from the precolate? What effect does it have on percolation?

The earlier views of the percolation of plant drugs was that fresh portions of menstruum continually forced those which immediately preceded them through the mass and finally out at the bottom of the apparatus,[1] this being a true displacement, each layer of menstruum acting as a piston upon those layers beneath it. The Boullays therefore termed it "the method of displacement" and the term percolation did not come into general use until later.

Vauquelin[2] proved the displacement of salt solutions from sand by fresh water and his experiments were repeated by Deane who verified his conclusions.

Rossenwasser[3] appears to have been the first to challenge in print the idea of displacement. He says that cell percolation depends upon osmosis, not on displacement and offers experiments in support of his views.[4] Guillermond[5] and Soubieran[6] had long before shown that alcohol cannot be displaced from a marc by water without some intermixture of the two liquids.

Experiments based on the displacement of liquids from sand offer little to parallel ordinary percolation. The difference in conditions is obvious; with such "marcs" as sand there is no absorption of menstruum or solution though there may be, and probably always is, adsorption to some extent. With cellular structures there is always absorption of the menstruum, consequently there is an attracting force between the fibre and the liquid which resists the effort of the fresh menstruum to wash out the absorbed liquid. To appreciate the magnitude of this force one has only to recall the fact that huge rocks may be split by driving a wooden wedge into some crack in them and then wetting the wood. The wood absorbs the water in spite of the enormous pressure exerted against the act by the rock and, swelling in consequence, shatters the stone.

Displacement is, however, one of the factors which govern the

[1] The Boullays, *Jour. de. Pharm.* 21, 1, (1835). Soubieran, This Journal, Vol. 8, 221, (1836). Duhammel, This Journal, Vol. 10, 1, (1838); Deane, *Pharm. Jour.* 1, 61, (1841). Graham, This Journal, 31, 354, (1859).

[2] Quoted by Deane, (v. s.).

[3] *Proc. A. Ph. A.* 1882, 519.

[4] *Proc. A. Ph. A.* 1885, 399.

[5] *Jour. de. Pharm.* 21, 349, (1835).

[6] This Journal, Vol. 8, 221, (1836).

percolating of the menstruum; with the force of gravity it serves to overcome the surface tension holding liquid between the drug particles and so assists the descent of percolate.

If the process of percolation were wholly one of displacement the absorbed menstruum would present no such problem as it now does. It would simply dissolve a certain fraction of the extractive and be completely replaced by a layer of fresher menstruum, itself moving to the next lower section of drug. It is not so displaced, however, as anyone may easily conclude after watching the descent of menstruum through a moistened drug packed in a glass percolator. The new menstruum fills up the air spaces between the swollen drug particles and part of it may be absorbed if the drug was not completely saturated with liquid when it was packed. The absorbed liquid does not appear to be disturbed.

The composition of the absorbed menstruum is, of course, variable for it will contain a large amount of dissolved extractive during the early part of the process and at the end is practically pure menstruum. However, it may vary considerably from the composition of the percolate especially where the menstruum contains any large percentage of water. The marc will exert a selective absorption in such cases with the result that more water than alcohol will be absorbed by the drug.[1] The solvent powers of this absorbed menstruum willl be different from those of the original menstruum and, consequently, the nature and quantities of the dissolved substances will not be the same in the two solutions.

I do not regard it as probable that the absorbed portions and the precolate liquid are consolute, that they freely mingle. The absorbed liquid is, for practical purposes, a solid body. It is a part of the drug being acted upon by the precolate precisely as we have been in the habit of thinking the drug was itself acted upon by the menstruum. It is much more likely that the extractive is first dissolved in the absorbed liquid whence it diffuses into the precolate which bathes each particle of drug while a further quantity of soluble matter goes into solution in the absorbed liquid. There may be some small diffusion of molecules of absorbed liquid into the precolate with concomitant replacement by molecules from the latter but this must be on so small a scale as to be negligible to all but the most minute scrutiny.

If there was a complete diffusion into the precolate or a displace-

[1] Cf. Patch, in discussion. *Proc. A. Ph. A.* 1892, 176.

ment of the absorbed menstruum we should find the conditions which Procter[1] assumed. Experimental evidence, however, disproves this contention and even in those rare cases where the second fraction of the percolate[2] contains more extractive than the first, an explanation may usually be found in the fact that the first portion has lain in the bottom of the percolator quite out of contact with the drug, at least in part, while the second fraction was macerating in contact with soluble material.

To the foregoing considerations may be ascribed the fact that Squibbs' repercolation process does not possess as great advantage over simple percolation as it would if we were dealing with displacement or "osmosis," and also the failures of complicated and ingenious vacuum and pressure apparatus may be due to this same cause.

Percolation does not depend upon "osmosis" except insofar as that term was used for "diffusion" by the early writers. Osmotic pressure, if it influences the process at all, serves to hinder rather than to facilitate the extraction, for it would operate to draw the menstruum into the cell instead of forcing solution out of the cell and, consequently, we should have to wait until the cells burst open from internal pressure before we could have dissolved extractive in the precolate. There is no evidence that this is the case; rather is it probable that the cell wall is so much altered in drying that it can no longer serve as a semipermeable membrane.

THE PRECOLATE.

The precolate is a heterogeneous mixture of solutions which fills the interstices of the packed drug from the upper layers to the stopcock. Its composition varies by infinitesimal degrees from pure solvent to partly saturated solution. Only rarely, if ever, is any portion of the precolate a fully saturated solution; this is shown by the fact that the first portions of percolate, that is, the most concentrated portions, seldom contain as much extract as the fluidextract made from the particular drug in question.

The character of the changes in the composition of the precolate from the upper to the lowermost portions is of considerable interest from the practical as well as the theoretical point of view. Lloyd[3]

[1] This Journal, Vol. 31, 317, (1859).

[2] Cf. Lloyd, This Journal, Vol. 50, 438, (1878).

[3] *Proc. A. Ph. A.* 1881, 498; 1882, 508; 1884, 410; 1885, 411. This Journal, Vol. 80, 39, (1908).

has devoted much attention to this question especially with reference to its bearing on precipitation in fluidextracts. The writings of Squibb,[1] Diehl,[2] and others present data which bears on this problem.

As the menstruum descends through the drug it dissolves the extractive which diffuses into it and its concentration increases. With this increase in concentration its solvent powers diminish so that the rate at which it extracts soluble material from the moist drug decreases while the loss of soluble material due to adsorption becomes greater.

All solutions are subject to adsorption, for contact with a surface leads to this under the proper conditions of surface tension. Increase of surface area and of concentration in solution lead to increased adsorption. This is a factor which opposes extraction and one which intimately concerns the composition of the precolate. Out of the great variety of classes of extractible drug constituents from the water-soluble proteins to the alcohol-soluble terpenes and resins, there is present in the percolate an extremely complex and variable mixture, the components of which differ in the degree to which they are adsorbed as well as in their relative solubilities and concentrations. In such a solution slight variations of temperature and pressure as well as gain of certain constituents by solution and part loss of others through adsorption may readily upset the nicely adjusted equilibrium and lead to precipitation within the percolator. Such a condition as this would lead to striking differences in different portions of the percolate.

Again, as the precolate descends the percolator and becomes more and more saturated, two things happen; its solvent power for more of the substances already in solution diminishes while its alcoholic strength decreases. The latter fact may so alter the quality of its solvent action that there may occur a solution in quantity of substances which were but slightly dissolved out of the upper layers of the drug. In certain cases this will result in a readjustment of the solution and precipitation may result. The net effect of such an occurrence is an actual transfer of soluble materials from the upper to the lowers layers of the percolator, the deposited matter being forced to wait for menstruum of proper quality before it can be redissolved and so extracted. The effect of mixing the first and last portions of percolate under such conditions is obvious.

[1] This Journal, Vol. 38, 109, (1866); 39, 289, 398, 513, (1867); 40, 1, (1868).
[2] *Proc. A. Ph. A.* 1878, 681; 1880, 424.

The rates at which the various constituents of a drug go into solution appear to differ materially; certain substances, especially those which are crystalline and of low molecular weight, diffuse more rapidly than cumbrous, amorphous compounds and so are found in larger quantity in the first portions of percolate than in later fractions. Our investigations of this most important subject have merely dipped below the surface. Squibb's work, quoted in detail below, has established the fact. In a drug like prunus serotina from which Power and Moore[1] isolated no less than fourteen constituents varying in character from a water-soluble glucoside to resin and phytosterol, the relative rates of extraction with the ordinary pharmacopoeial menstruum must be very diverse, and to this is added the possibility of the complete hydrolysis of the glucoside yielding hydrocyanic acid which, by altering the hydrogen-ion concentration of the solution, might cause precipitation of the resin.

Moreover, as the menstruum proceeds downward and the dissolving of the extractive decreases in extent, the rate of solution for any individual substance must be diminished, but there is no reason to expect that the rates of solution of all the soluble constituents are affected in the same proportion. Consequently, this is another condition which may vary the composition of the precolate.

In addition, the mutual effects of dissolved substances upon each other and upon soluble, but undissolved, material affect the composition of the precolate. Certain substances are much less soluble in solutions of some other compounds than they are in the pure solvent. Glucosides are less soluble in slightly acid liquids than they are in neutral or alkaline media. Terpene oils are quite insoluble in liquids which contain inorganic salts. Under such conditions the less soluble constituent would be obliged to remain in the marc until the greater part of the precipitant is extracted before it may be dissolved. In a case of this kind we should have qualitatively different solutions in the upper and lower regions of the percolator.

Contrariwise, many constituents of drugs are extractible by solvents in which they are really insoluble because of the presence in solution of other substances which modify their solubility. Sugars are readily extracted by alcohol although they are, as a class, but little soluble in that liquid. Glucosides which are insoluble in water may, nevertheless, often be extracted by that solvent. Gitalin,[2]

[1] *J. Chem. Soc.* 95, 243–261, (1909).

[2] Meyer, *Arch. exp. Path. u. Pharm.* 81, 261, 288, (1917).

from digitalis is readily soluble in chloroform but not so in water, yet owing to the presence of tannins in the leaf, it may be perfectly extracted therefrom by water but cannot be extracted by chloroform. The glucoside of oleander leaves, oleandrin,[1] although practically insoluble in water is readily and completely extracted by cold water owing to the modifying influence of a phenolic glucoside present which is soluble in water. Jowett[2] reports that emodin, though only slightly soluble in water, is extracted from cascara sagrada by an aqueous menstruum, and Squibb[3] stated that, while buchu could be perfectly extracted by dilute alcohol, the extract obtained by evaporating the percolate will not redissolve in dilute alcohol but requires the strong solvent. Such experiences are everyday occurrences in the manufacture of fluidextracts.

The effect of temperature on the composition of the percolate has been investigated by Norris[4] and Smith[5] who find that the percolate obtained at the higher temperature contains somewhat more extract. Smith reported that the rate of extraction of alkaloids is not greatly affected by increased temperature.

The great factor in determining the composition of the precolate is time. It is certain that, as percolation is ordinarily conducted, not enough time is allowed for equilibrium between the marc and the solution to be reached. The net effect of this is that those constituents which are quickly soluble are dissolved out while others, just as soluble but more slowly dissolved, are extracted in a fraction of their possible amount only and so are stretched through a greater volume of percolate than is necessary or desirable. The composition of the percolate will vary qualitatively according to the time it has been in contact with the drug. Several of the older writers seem to have thought a free flow of percolate desirable because they disapprove certain manipulations which "interfere with percolation" and advocate measures designed to remove impediment to rapid descent of the menstruum. I believe that such ideas are founded upon false principles; that the rate of flow of percolate is not the essential factor but that the rate of extraction is and the flow of percolate should be adjusted to yield as concentrated a liquid as the time at the

[1] Straub, *Arch. exp. Path. u. Pharm.* 82, 327–343, (1918).
[2] *Proc. A. Ph. A.* 1904, 288.
[3] In discussion, *Proc. A. Ph. A.* 1880, 550.
[4] *Proc. A. Ph. A.* 1898, 684.
[5] *Proc. A. Ph. A.* 1897, 245

operator's disposal will permit. Certainly, such a procedure will amply compensate in elegance and permanence of product.

(*To be Continued*)

WHO INVENTED THE TALL, NARROW PERCOLATOR?

By George M. Beringer, Ph.M.

Camden, N. J.

The historian is concerned in determining to whom credit should properly be given for each discovery, invention or advance made in our knowledge. The history of pharmaceutical products and of the apparatus and the processes used by pharmacists has not received the careful study that it merits and to determine the question of priority in the development of these will often times require critical review of the data and literature available. The longer the delay in settling questions that are involved and mooted the more difficult of settlement they become.

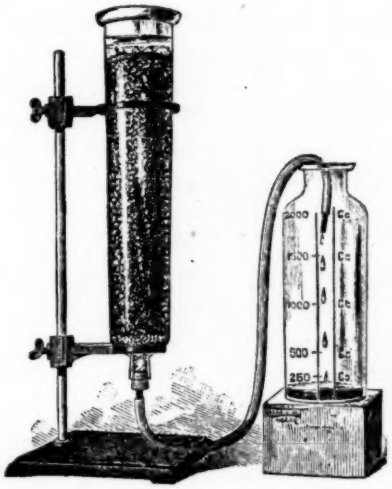
Pharmaceutical literature and the catalogues of apparatus manufacturers very generally speak of the "Oldberg" and the "Cylindrical" percolator, and credit is given to the late Prof. Oscar Oldberg for having originated this type of percolator. From the writer's study of this question he is convinced that neither the word "cylindrical" nor the appellation "Oldberg" in this connection is correct.

Reference to the original displacement apparatus of Boullay (see page 772) shows that the body or tubular portion of the percolator was really cylindrical but not proportioned in height and width to what is now accepted as the best dimensions for percolation. The orifice of the Boullay apparatus was of the funnel type with slanting sides and without the usual shoulder above the orifice of the percolator that has since been commonly adopted.

Upon referring to the original paper of Prof. Oldberg, as published in the *Proceedings* of the American Pharmaceutical Association for 1884, it is to be noted that the title thereof was "A Set of Standard Dimensions for Simple Percolators." In his paper he distinctly states that "I propose to summarize the conclusions to be derived from the able and exhaustive studies of Dr. Squibb and

Professors Diehl, Lloyd, Remington and others," and further states "there will be nothing new in the propositions here submitted." He proceeds to review the various processes of percolation, simple, re-percolation and fractional percolation.

The primary purpose of his paper, as set forth in the title, was a study of the best dimensions for simple percolators. He concludes that the " 'tall and narrow' percolators—considerably taller in proportion to their diameter than any heretofore obtainable on the



The Oldberg percolator as described in 1884.

market—are necessary to secure the proper exhaustion of the drug with a moderate quantity of menstruum, simple percolation being the process followed," and continues in the following language: "The sole object of using a tall and narrow percolator is to increase the height of the column of drug and menstruum in proportion to their mass."

After setting forth in a tabular statement the dimensions of the "standard percolators" used under his supervision in the pharmaceutical laboratory of the Chicago College of Pharmacy, he lays down as the rule for the preparation of these "that the total depth of each percolator is uniformly 5 times its large diameter and 6

times its small diameter. These percolators are, therefore, nearly cylindrical." This latter quotation proves that Dr. Oldberg himself did not apply the name "cylindrical percolator" to this type and recognized that they were not cylindrical.

It is not the writer's purpose to detract in the least from the credit due to Dr. Oldberg for formulating this rule for standard percolators of this type, nor even to intimate that he personally

The Diehl percolator as described in 1879.

was responsible for the attaching of his name to this type of percolator. However, when a critic studies, in the *Proceedings* of the American Pharmaceutical Association for 1879, the "Second Report on Fluid Extracts," by Prof. C. Lewis Diehl, he is forced to conclude that Dr. Oldberg had full knowledge of this contribution and followed in his paper the arguments advanced five years prior by Prof. Diehl.

In this communication Prof. Diehl was presenting his

study of the process of fractional percolation and whether it possessed any advantages over simple percolation properly carried out, and concluded that the object aimed at in fractional percolation could be obtained by simple percolation "if we increase the height of the column without increasing its diameter." In order to perform his experiments he states: "Being well aware, however, of the difficulties attending the percolation of high columns of vegetable powders, and particularly of narrow columns of such, I had some glass percolators constructed which, while of the same diameter at the upper and lower end as those ordinarily constructed, should be twice the usual height."

The figure illustrating his conception of a tall, narrow percolator for this purpose is reproduced herewith.

It is evident from these quotations that Dr. Oldberg followed very closely the ideas of Prof. Diehl and repeated substantially the latter's recommendations as to the approved type for percolators.

As a fact established by historical records, Diehl should be given credit in the pharmaceutical literature as the inventor of this form of percolator.

The writer is aware that, although Prof. Diehl made no published claims regarding the priority of his paper, he nevertheless felt rather keenly that credit had not been given where it was justly due. In a heretofore unpublished letter he wrote, under date of December 9, 1910:

"It does not take long to forget what has been done in previous years, and we daily discover, as new, facts which years ago have been practically demonstrated.

"How little time it takes to forget, or to overlook observations or recommendations made, is exemplified by the question of tall, narrow percolators recommended by me for preparing fluidextracts (and for extraction by percolation in general). Take a look at the percolator, Fig. 67 on p. 729 of my report in the *Proceedings* (American Pharmaceutical Association) 1879, and then compare with the percolator described and illustrated by Prof. Oldberg in the *Proceedings* 1884, pp. 388–392, which is now generally designated as the "Oldberg Percolator." Leaving the exact shape out of consideration, does not this open a question of precedence regarding the suggestion of 'tall narrow percolators;' and yet it had taken but a short five years to practically obliterate any modest claim I may have held for the suggestion made?"

ABSTRACTS FROM THESES.*

PRESENTED BY STUDENTS OF THE PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE.

EMULSIONS OF BENZYL BENZOATE.

The extensive use of Benzyl Benzoate and its disagreeable taste has given the pharmacist an opportunity to prepare palatable forms for use by physicians.

Edwin T. Brown, in his Thesis prepared in the Pharmacy Laboratory, has shown that an emulsion is readily prepared by the use of the commonly employed emulsifying agents such as acacia and tragacanth, but that the best results followed the use of tragacanth, 2 Gm. per 100 Cc., in a 20 per cent. emulsion of benzyl benzoate.

He also tried many flavors, including varying proportions of aromatic elixir of eriodictyon, "aromol," 10 and 20 drops per 100 Cc.; methyl salicylate and oil of cinnamon, each 12 drops per 100 Cc.; oil of cinnamon, 12 drops, methyl salicylate 18 drops per 100 Cc. of emulsion; methyl salicylate, 10 drops, oil of sassafras, 8 drops, and oil of sweet orange 12 drops per 100 mils; 12 drops each of the same three oils and 8 grains of vanillin per 100 Cc. of emulsion.

The conclusion reached by Mr. Brown is that 20 drops of "aromol" or 12 drops each of methyl salicylate, oil of sassafras and sweet orange are the best flavors tried, although even these large amounts of aromatics fail to completely cover the disagreeable taste of the benzyl benzoate.

NOTES ON THE ASSAY OF PHOSPHORIC ACID.

The U. S. P. IX assay for phosphoric acid has proven unsatisfactory in the hands of many chemists. This assay is inconsistent in its conclusions, and therefore inaccurate because of the varying amounts of zinc oxide, which may be added, and which make up a part of the final volume from which an aliquot portion is taken for titration.

Mr. H. L. Cline in a thesis prepared in the Chemical Laboratory proposes to overcome this difficulty by filtering the liquid, after neutralization with zinc oxide (using a Gooch crucible) washing the precipitate with water until free from silver nitrate and adding distilled water to make the total volume measure exactly 100 mils. An aliquot portion of this solution is then titrated with tenth-normal

* Prepared by E. Fullerton Cook, Ph.M. and A. B. Nichols, Phar.D.

potassium sulphocyanate solution in the usual manner, and calculated from the per cent. of phosphoric acid.

By eliminating the variable factor, the zinc oxide, concordant results have been obtained in a number of assays in the hands of different operators.

MODIFIED METHOD FOR PREPARING ETHYL NITRATE.

In a thesis prepared in the Pharmacy Laboratory, Charles H. Pitt states the use of a separatory funnel for the collection of ethyl nitrite as it floats upon the surface of the saturated sodium sulphate solution, as directed by the U. S. P. IX, has not proven satisfactory in the hands of many operators. The chief objection is the large loss from evaporation during the process. To overcome this, where the distillation method is not available, Mr. Pitt has devised an apparatus which largely prevents loss from evaporation. He proceeds as follows:

Two large flasks are placed in ice-baths, and the one closed by a doubly perforated stopper. Through one perforation a thistle tube (or a glass tube connected at the top by a piece of rubber hose with a small funnel) is inserted, so that it extends almost to the bottom of the flask. A second tube, bent at a right angle an inch above the stopper is inserted in the other perforation and just passed through the stopper. This tube is again bent at a right angle and the outlet end inserted in the second flask, extending almost to the bottom.

The reaction between the sodium nitrite, alcohol, and sulphuric acid is now carried on as usual, in the cold first flask, and when the strata of ethyl nitrite has collected on the surface of the mixture in the flask, more water is carefully poured in, through the funnel tube, until it forces the ethyl nitrite over into the second flask, through the connecting tube. Now the tubes are reversed, and the washing with sodium carbonate solution accomplished in the second flask the ethyl nitrite being subsequently returned to the first flask by adding water as before, the first flask having, of course, been cleaned. It is now washed with cold water as before, and, when finally treated with potassium carbonate is ready for dilution with alcohol for the preparation of the spirit.

Distillation flasks, with a side tube, may to advantage replace the usual Florentine or Erlenmeyer flasks whereby the contact with a rubber stopper is avoided.

By this method practically all loss by evaporation is avoided

and the preparation of ethyl nitrite made possible with very simple apparatus.

FREQUENTLY USED SATURATED SOLUTIONS.

The dispensing pharmacist is frequently called upon to prepare saturated solutions of certain salts, and is accustomed to depend upon the solubility statements of the Pharmacopoeia as a guide. These figures are valuable so far as the information goes, but do not show the volume of the completed solution, and therefore are an incomplete guide where a definite volume of a saturated solution is to be prepared.

Lewis G. Freeman in a thesis prepared in the Pharmacy Laboratory has undertaken experiments to supply these desired figures for several salts often called for in the form of saturated solutions. In each instance a definite weight of strictly U. S. P. salt was taken (10 Gm.) and the solubility checked in three ways. First the exact amount required for solutions, as stated by the U. S. P., was added, the mixture frequently agitated at 25° C., in a tube, graduated to tenths of a Cc., until solution resulted. It was necessary in all cases to add slightly more water, to dissolve the salt than stated by the Pharmacopoeia. When completely dissolved, the final volume was noted.

By the second method the salt (10 Gm.) was dissolved in the specified volume of water, with the aid of heat, but a slight additional amount of water was required to prevent crystallization on cooling. Again the volume was noted.

In the third experiment an excess of the salt was agitated with distilled water, at 25° C., until the solution was saturated, the mixture filtered, and a definite volume (10 Cc.) carefully evaporated. The weight of the salt obtained was then calculated for a comparative basis. The average of these figures was used in the following results.

The figures showing the amount of salt and water to take for making 100 Cc. 1 fluidounce, and 16 fluidounces of a saturated solution are calculated from the experiment with 10 Gm. of salt.

Potassium Iodide.

KI taken, 10 Gm....	99 (98.52) Gm.	451 (450.47) Grs.	1 Lb. av. 208 Gr.
Water taken, 7.2 Cc.	71 (70.93) Cc.	340 (340.39) Min.	11 Fl. Oz. 166 Min.
Resulting volume, 10.15 Cc.....	100 Cc.	1 Fl. Oz.	16 Fl. Oz.

Sodium Iodide.

NaI taken, 10 Gm...	110 (110.13) Gm.	502 (502.4) Gr.	18 Oz. av. 163 Gr.
Water taken, 5.5 Cc.	61 (60.57) Cc.	291 (290.68) Min.	9 Fl. Oz. 331 Min.
Resulting volume, 9.08 Cc.....	100 Cc.	1 Fl. Oz.	16 Fl. Oz.

Magnesium Sulphate.

$MgSO_4$ taken, 10 Gm.	63 (62.9) Gm.	287 (286.99) Gr.	10 Oz. av. 217 Gr.
Water taken, 10 Cc..	63 (62.9) Cc.	302 (301.87) Min.	10 Fl. Oz. 30 Min.
Resulting volume, 15.9 Cc.....	100 Cc.	1 Fl. Oz.	16 Fl. Oz.

BACTERIA IN (SO CALLED) SOFT DRINKS.

LOUIS GERSHENFELD, PH.M., B.SC.,

PHILADELPHIA, PA.

Scientific investigation has given ample proof that there is a close connection between the spread of disease and the water that is used in a community. A pure water supply is of first importance in the prevention of disease and in the conservation of public health.

From time to time, there has been considerable discussion over the superiority of the chemical or bacteriological examination of water. This has been quite useless, for though a bacteriological analysis may be shown to be of greater importance, a chemical examination will nevertheless detect the presence of certain chemical substances, from the relative amounts of which, an inference may be drawn as to the existence of pollution with human or animal excreta, or, in some instances, with poisonous or injurious compounds. It is therefore apparent that both examinations should be carried out.

It is with this in mind, that communities are compelled either by state or other recognized authority, to determine the purity of their water supplies, by performing bacteriological and chemical examinations at frequent intervals.

It is, of course, evident that such steps taken for the careful guarding of our water supplies are justifiable. Furthermore, it is apparent why sanitarians soon became interested in the control of milk, cream, ice cream, ketchup and other food supplies, so as to determine that these products will not introduce disease into the numerous communities. But there seems to be one class, the soft drinks, used so extensively, that has been sadly neglected by the

sanitarian. In fact many use soft drinks, bottled or otherwise, almost exclusively for drinking, while the potable water supplied is used for every purpose other than drinking.

The writer is aware that some municipalities attempt to guard the market supply of soft drinks in behalf of the health of their respective communities, but he is assured that effort along these lines is indeed small. There is no doubt that no other product is supplied to the public in such large quantities, as are soft drinks.

A *pure* soft drink is just as essential to the prevention of disease as is potable water, milk, etc. At present, many behind the pure food movement, carefully investigate these products, to be assured that saccharine or an injurious coal tar coloring preparation is not being used. A chemical examination to indicate pollution with animal excreta is not warranted or necessary, due to the fact that a potable and chemically pure water is furnished to the plant for the manufacture of the numerous products and the finished preparation does not stay around long enough to show any apparent ageing or decomposition.

The chemical methods of examining soft drink supplies, as previously mentioned, will not detect the presence of bacteria, much less assist in their identification. A bacteriological examination of such water will, however, reveal the number and in some instances the types of bacteria in a given volume. The fact should not be overlooked that even though a potable water was used, the finished product may nevertheless be highly contaminated, due to the carelessness and unsanitary methods used in the manufacture of the preparation.

The bacteriological examination of soft drinks is a more direct and delicate test, both as to the sanitary operation of the plant, as well as on the factors, that have an important bearing as to the value of the finished product. An analysis of the bacterial content of a soft drink will quickly reveal the hygienic conditions, prevailing at the time of the manufacture of the particular preparation. Early examinations may prevent epidemics, as they act as a check. It would be advisable to make an inspection of the plant, to determine the cause of the pollution, and to advise the remedial measures to correct any evil that may exist.

It has been the privilege of the writer to guard from a sanitary standpoint the making of soft drinks, and it is for this reason that he advises all manufacturers, not only of soft drinks but of all bottled

water to protect themselves, by carefully supervising the manufacture as well as the finished preparations. It is advisable that they start early to control the bacterial content of their samples, before they will be compelled to do so, as there is no doubt that in the near future, legal requirements will necessitate such supervision.

A community has a right to demand that whatever qualities soft drinks may claim or may possess, these should be secondary to cleanliness and it should be the duty of those who guard the health of the community to determine whether such products are free from contamination. The public should demand this as they have the right to expect it. Many laymen are under the impression that such strict supervision is at present being exercised by proper authorities.

The water used in the manufacture of the soft drinks in plants, under the writer's observation, was usually found to be potable. The danger of contamination is due more to the careless washing of the containers, or the introduction of a contaminated flavoring syrup, or to minor details carried out during the operation. Actual inspection of the plant during every stage of manufacture, together with bacteriological examinations of all ingredients entering into the preparation of the beverage will lead to a determination of the responsibility for any unsuitable product. In the long run, such inspections and examinations save untold worry and considerable expense.

An artificially carbonated water prepared under cleanly conditions, will usually show a low bacterial content. The writer carbonated a number of samples on one occasion. The containers were cleansed properly, the flavoring syrup was low in bacteria, and all other procedures were guarded as they should be by any one familiar with the simple technique of filling the bottles. The bacterial content of the finished preparation was lower Cc. per Cc. than was observed in the water used in preparing the product.

To actually show what the condition is, the writer obtained 15 samples of different brands of soft drinks. Many of these were bought during the months of April and early May, and obtained from lots that were delivered, in most instances, in his presence. He was thus assured, that the samples represented the finished products as sent out from the plants of the various manufacturers and did not represent samples that were allowed to incubate at room temperature or exposed to heat in the retail stores.

Of the fifteen samples, six, or 40 per cent., were found to contain

B. Coli in 10 Cc. portions. Lactose Bile and Lactose Bouillon were used for the presumptive test for B. Coli. Three 10 Cc. portions were used. In all of the six reported instances, B. Coli were isolated from the fermentation tubes.

One gave considerable gas with all three 10 Cc. portions. No B. Coli were found, but B. Welchii, another sewage bacterium, was present.

In the total bacterial counts on agar at 37° C. after 48 hrs. incubation, two showed counts lower than 100 per Cc. Three samples showed the presence of less than 300 bacteria per Cc. Three others had a bacterial content ranging between 500 and 1000 per Cc. The other 7 had a count of over 1000 bacteria per Cc. The bacterial count on agar at 20° C. in most all of the foregoing samples was somewhat higher than the 37° C. counts.

Some of the organisms found were staphylococci; short and long, chain streptococci; B. Coli; B. Welchii; B. Cloacae; B. Subtilis; B. Mycoides; B. Mesentericus Vulgatus; diphtheroids; streptothrices and molds.

The occurrence of some of the foregoing does not speak well as to the cleanliness of the samples or of the desirability of indulging constantly in such drinks.

Facts such as these give weight to the opinion, entertained by the writer, that more attention must be given to the sanitary aspect of this whole problem.

THE PROFESSOR—AS YET UNSTANDARDIZED.*

By J. W. Sturmer, Phar. D.,
Philadelphia, Pa.

According to Garfield, Dr. Hopkins seated on a log, constituted an institution of higher learning adequately equipped to afford a liberal education to the student fortunate enough to occupy a seat on the same log with this learned doctor.

Higher education has developed marvelously since Garfield coined his famous phrase in laudation of Dr. Hopkins. The log is now represented by pretentious buildings, with commodious lecture rooms, excellent laboratories, well-stocked libraries, and the various appurtenances and aids, such as projection apparatus, charts, etc., which the modern instructor finds helpful in transmitting

* Read at the Washington meeting of the American Conference of Pharmaceutical Faculties, May, 1920.

knowledge to his more or less receptive students. Millions have been invested and invested to good purpose in physical equipment for education. So important is this equipment deemed that this Conference has seen fit to fix a minimum standard in this respect for the schools and colleges of pharmacy which constitute its membership. And who would contend that this standard which the Conference has set, is without value?

But educational bodies including the Conference have gone further. They have in a way standardized the student—at least they have set up certain entrance requirements to ensure, on his part, a proper preparation for his college work. This also was good common sense and made for real progress in pharmaceutical education.

The evolution of the log having eventuated so splendidly and the matter of entrance requirements being definitely settled there are those who now make inquiry why this very conspicuous educational advancement has not brought results which are commensurate with the progress made. We may answer and furnish evidence to substantiate our statement that there has been in very fact a considerable gain. Not that the best men of our present classes are necessarily better than the best men of the past—but the average is better and the poorest of the present-day graduates show a marked improvement over the poorest of the earlier classes. Despite this distinct gain there is, to be sure, still much room for improvement in our schools of pharmacy. We are convinced, however, that the next conspicuous advance in the schools of this Conference will not result primarily from further elaboration of material equipment, nor will it be due to the adoption of still higher entrance requirements; it will result rather from improvements in the curricula and in the development of higher efficiency in the art of teaching. After all, the professor is the all-important factor in the educational mechanism. His personality will compensate for a lack in teaching facilities; his inefficiency can render almost worthless the finest equipment.

The particular service of this Conference has in the past been largely in the matter of fixing standards—standards for equipment, standards for entrance requirements, standards for the faculties from the standpoint of numerical strength. And when we proceed to take up seriously the most complicated educational problem of all, namely the professor, the first step suggested will no doubt be the establishing of standards with reference to his academic titles,

and it will be decreed that a professor shall possess certain scholastic qualifications. That such standards are both feasible and useful is evidenced by the fact that requirements as to degrees attained have for years formed a part of the policy of many educational institutions in the matter of selecting new members for their faculties.

But it must be remembered that while the basic principle underlying such a policy is sound enough, scholastic standards by themselves cannot ensure an efficient faculty, for the proud possessor of a doctorate, notwithstanding the etymology of the word, is not necessarily a teacher and may in fact never, because of certain unfavorable character traits, develop into a good teacher. Nor can we be sure that the promising young post-graduate who has planned and has executed a creditable piece of research has thereby proven his ability to teach classes. Indeed, research ability precious as it is and necessary for the advancement of science, may be possessed by a person wholly unfitted temperamentally to deal successfully with students. Sometimes, to be sure, we find high research ability and the essential qualifications of a teacher in the same person. But it is but seldom that nature so lavishly endows one of its children.

Having disposed of the relatively simple matter of academic standards for the professor, the Conference may next investigate his ability as a teacher. Has he the power of clear exposition—the ability to develop his subject in a logical manner? Has he mastered the technique of lecture demonstrations? Does he know—and does he proceed on the basis of such knowledge—that if experiments are not properly timed, or if the point to be demonstrated is obscured by over-emphasis of certain details, the student is confused rather than helped by this accessory to the lecture? Does he perpetrate that most serious yet common fault of using technical terms unfamiliar to the student or does he avoid such terms until they can be explained with proper connections so that the student's mastery of the nomenclature may develop with his progress in the science? Alas, who has not heard a biology lecture which seemed to be in a foreign language, and wondered how there can be so much verbiage about so little foliage. Can he capitalize his sense of humor and give human interest to his subject without falling into a hopeless condition of anecdotage which renders him ludicrous rather than humorous. We learn to teach by constant trial and by observing the methods of our elders—in this way rather than by following rules and precepts. But does our young professor know that the success-

ful teacher has not only developed methods which are inherently and intrinsically good but has also attuned them to his own personality?—or has he fallen into the error of slavish imitation? Is he a mere automatic transmitter of knowledge, or has he a spark of that marvelous fire which inspires others to become willing and productive workers in the field? For this is after all the most essential qualification of a good teacher.

If we look back over the list of teachers with whom we have been in personal contact, we are rather surprised to find that those who have scored the most pronounced success are not necessarily the most erudite of the lists nor the most productive investigators nor even the men employing the most approved pedagogic methods, but those inspirational personalities who imparted to their students their own enthusiasm and their own love for the work. If the results of teaching are to be measured by the productive workers produced rather than by the number of correct answers the students can give in the final examination—and this is the real criterion—it is the inspirational teacher who must be accorded the highest place in the teachers' hall of fame. And let us remember, that no teacher can inspire his students unless he is convinced of the deep and lasting importance of his subject.

Pharmacy in particular has suffered severely at the hands of its iconoclastic friends and its apostles of negations—who contend that medicine is the science of diagnosing disease—that cures are impossible—that therapeutics teaches the futility of drug medication—that vegetable histology deals with intercellular air spaces—that pharmacy is a collection of cook-book recipes for the preparation of useless concoctions. Let us remember that we cannot kindle the enthusiasm of our students with epigrammatic negations. Unless the professor of a pharmacy school believes in pharmacy as a necessary and important part of the world's work, his influence will be positively harmful. So we can rightfully ask also does the professor who has met our other requirements also meet this: does he subscribe to the articles of faith of true pharmacy? Does he firmly believe that he is training his students to become useful citizens who will earn their daily bread in the service of their fellow men?

In standardizing the professor, let us attack the problem as a complicated one involving the human equation. Let us not be too mathematical, too mechanical. Let us not overlook the potential Dr. Hopkins and accept the mere bookworm.

Let us deal with the professor in a broad and sympathetic way. He is the all-important factor in our educational scheme which we have so laboriously builded. With him rests largely the future of pharmacy, for it is he who deals with the on-coming generation of pharmacists. Let us standardize the professor by all means; but let us do it wisely.

THE EFFECTS OF PROLONGED HEATING AND OF AQUEOUS EXTRACTION ON OPIUM.

By Alex. M. Macmillan and Alfred Tingle,

Ottawa, Ont., Canada.

INTRODUCTION.

The work of H. A. Annett and Hardayal Singh[1] on the change of morphine content produced by heating opium was of such interest to the Customs and Inland Revenue Laboratory at Ottawa that it was found desirable to check the results and endeavor to confirm them. We also wished to extend the scope of the observations recorded and we believed that we could improve on some points of procedure, eliminating or minimizing certain possible sources of error.

Our conclusions differ from those of these previous authors. We cannot consider that the variations in experimental conditions are wholly responsible for the different results obtained. We should have preferred to carry our work much further, so that it might be final rather than tentative. Both of us having left the laboratory where we undertook this investigation, and neither of us being in a position to continue it alone, we have decided that it is best to publish these results as they stand, leaving the last word on the subject to some other worker.

H. A. Annett and Hardayal Singh used the B. P. method for their estimations of morphine. While as good as any method then available, it is open to three objections: (1) The results admittedly may vary as much as 0.5 per cent. in either direction. (2) Its adoption made it necessary to add enough water to the heated material to bring it back to its original weight. Justification for such action

[1] *Jour. Soc. Chem. Ind.*, 37: 315T, 1918.

rests on the unproved assumption that the observed loss of weight is entirely due to loss of moisture pre-existing in the opium. (3) The published discussion on their paper[1] shows that it is doubtful whether the B. P. method has the same degree of accuracy for heated as for unheated opium.

We believe that we have overcome these objections in our own work by using the method of estimating morphine devised by one of us (T)[2] which is equally applicable to opium in any form irrespective of previous heating and regardless of its moisture content for which no "correction" is necessary.

The claim has already been frequently made that water alone, even when boiling, will not extract all the morphine from opium[3] and that an aqueous extract of opium loses morphine when boiled or evaporated on the water bath. With the material at hand we intended to enquire further into these matters. Our actual results do not go very far for the reason already mentioned, but at least confirm those of previous workers.

EXPERIMENTAL.

The Effect of Prolonged Heating on Opium.—Each batch of opium was prepared by being air-dried, powdered in a glass mortar, and passed through a 40-mesh sieve. The resulting powder was heated at 60° C. for 24 hours, then transferred to a can with a tight (but probably not air-tight) lid in which it remained till the working samples were withdrawn. These were all taken at the same time each consisting of 6 Gms. weighed on balanced watch glasses. Those which were not to be immediately analyzed to establish the morphine content of the material before heat treatment were placed in a Frea's electric oven (at atmospheric pressure) heated at 98°–100°. These heated samples were re-weighed at intervals and at predetermined times samples were withdrawn from further heating, the morphine content then being determined by the method already mentioned. Two batches of opium were experimented upon, one being of Persian the other of Indian origin. The results are tabulated below.

[1] *Loc. cit.*

[2] *Amer. Jour. Pharm.*, 90: 851, 1918.

[3] Debourdeaux, *Bull. Sci. Pharm.*, 17: 382, 1910.

TABLE I.—THE EFFECT OF HEAT ON PERSIAN OPIUM AS TO WEIGHT AND MORPHINE CONTENT. ASSAY OF AN UNHEATED SAMPLE SHOWED MORPHINE 9.35%.

Time of Heating (Hours).	Weight of Opium after Heating (Grams).		Weight Lost by Opium (Per Cent.).	
	Sample No. 1.	Sample No. 2.	Sample No. 1.	Sample No. 2.
0	6.0000	6.0000	....	....
24	5.8112	5.8005	3.14	3.32
48	5.7668	5.7596	3.89	4.00
72	5.7410	5.7460	4.31	4.23
96	5.7260	5.7174	4.57	4.71
192	.....	5.6674	....	5.54
288	.....	5.6360	....	6.07
Percentage of morphine found at end of heating.			5.98	5.98

TABLE II.—THE EFFECT OF HEAT ON INDIAN OPIUM AS TO WEIGHT AND MORPHINE CONTENT. ASSAY OF TWO UNHEATED SAMPLES SHOWED MORPHINE 6.56% AND 6.66%.

Time of Heating (Hours).	Weight of Opium after Heating (Grams).					Weight Lost by Opium (Per Cent.).				
	Sample No. 3.	Sample No. 4.	Sample No. 5.	Sample No. 6.	Sample No. 7.	Sample No. 3.	Sample No. 4.	Sample No. 5.	Sample No. 6.	Sample No. 7.
0	6.0000	6.0000	6.0000	6.0000	6.0000	....	....	....	....	....
24	5.8243	5.8355	5.8892	5.8846	5.8835	2.93	2.74	1.84	1.92	1.94
48	5.8138	5.8215	5.8257	5.8236	5.8012	3.10	2.97	2.90	2.94	3.31
72	5.7843	5.7775	5.8107	5.8076	5.7967	3.59	3.71	3.15	3.20	3.39
96	5.7748	5.7665	5.7592	5.7801	5.5527	3.75	3.81	4.01	3.66	4.12
192	5.7143	5.7235	5.7087	5.7256	5.7057	4.76	4.61	4.85	4.57	4.90
288	.....	5.7020	5.6892	5.6961	5.6797	....	4.97	5.18	5.06	5.34
384	.....	.....	5.6747	5.6651	5.6657	....	....	5.42	5.58	5.74
480	.....	.....	.....	5.6531	5.6402	....	....	....	5.78	5.99
576	.....	.....	.....	.....	5.6277	....	....	....	....	6.20
Percentage of morphine found at end of heating						6.40	5.64	5.54	5.13	4.52

The Effect of Prolonged Heating on Crystallized Morphine.—While it has no necessary bearing on the changes undergone by such a product as opium, we believed there would be some collateral interest in making a careful measurement of any alteration which morphine might undergo when heated. From a specimen of very pure crystallized morphine 1 gram was exactly weighed on a balanced watch glass. It was then heated in the electric oven between 98° and 100° C. and weighed at intervals.

Time of Heating (Hours).	Weight of Sample (Grams).	Total Loss of Weight (Grams).
24	0.9406	0.0594
48	0.9406	0.0594
72	0.9406	0.0594
96	0.9407	0.0593
192	0.9408	0.0592

The loss of 0.0594 corresponds exactly to the weight of the theoretical water of crystallization. After being heated for 96 hours a yellow tinge was observed in the previously white powder. This became decidedly deeper when the heating had been prolonged for 192 hours.

The Extraction of Morphine from Opium by Hot Water.—An experiment was made on the Persian opium previously used, to show (1) how much morphine would remain undissolved by hot water and (2) how much morphine would be destroyed under the conditions of extraction.

A sample weighing 6 grams was extracted with hot water in a Soxhlet Extractor till the overflowing liquid showed no further color. This involved boiling for about 16 hours. The exhausted residue was carefully collected and dried first in the air then in a desiccator. Determinations of morphine were then made on the whole both of the exhausted residue and of the extract.

	Total Weight of Morphine Found (Grams).	Percentage of Morphine on Original Weight of Opium.
In exhausted residue	0.0100	0.17
In concentrated aqueous extract	0.4965	8.27
Morphine lost (by difference)	0.0545	0.91
Total	0.5610	9.35
Found by assay of original opium	0.5610	9.35

DISCUSSION OF RESULTS.

Loss of Weight by Opium When Heated.—Our results show a steady loss of weight when opium is heated. There is no sign of constancy having been attained even after 576 hours at 98°–100° C. Different samples agreed very fairly among themselves considering that the material was weighed on open watch glasses and is always somewhat hygroscopic. On these points we are at variance with Annett and Hardayal Singh,[1] who claim to have obtained

[1] *Loc. cit.*

practically constant weights after 192 hours. Our Sample No. 7 (Table II) shows a loss of more than 1 per cent. in the period 192 to 576 hours. These workers also assert that opium is practically non-hygroscopic when dried at about 100°. On this minor point also our results are not parallel. As would be expected, we are able to agree that the greatest loss of weight takes place in the first or second day of heating.

Change in the Morphine Content of Opium When Heated.—Our results point to a sharp difference between Persian and Indian opium. Table I shows that the Persian opium lost more than 30 per cent. of its morphine on being heated for 96 hours, but lost no more when the heating was continued to 288 hours. On the other hand Table II shows the Indian opium as having lost only about 3 per cent. of its morphine on being heated for 192 hours, but as losing progressively and heavily till it had lost about 30 per cent. on 576 hours' heating. Again we differ from Annett and Hardayal Singh, who claim to have found an increase in the morphine content from 264 hours to 288 hours' heating, though we agree with them (as regards Indian opium on which alone they worked) that the first period of heating causes no great change but that once started it proceeds regularly up to 264 hours. None of their experiments cover a longer period than 288 hours. It seems probable that the slight rise in morphine-content which they report is due solely to an analytical error. Their results differ markedly from those we have obtained on Persian opium.

Our conclusion is that many more comparative experiments are necessary before it can be definitely stated that Indian and Persian opium differ in their behavior towards heat. We consider it as proved, however, that some samples of opium loose a notable amount of morphine before all the moisture has been expelled. We believe that while further investigation is called for, it would be well to take into consideration the facts already shown in planning any assay of opium.

The Effect of Prolonged Heating on Crystallized Morphine.—The free alkaloid proved to be much more stable than we anticipated. While it lost its water of crystallization during the first day of heating, no further change could be detected till it had been heated for four days. Even when heated for eight days it had only gained 0.2 Mg. over its anhydrous weight and any change in its basicity was not appreciable. After such a period of heating opium, itself, had shown a decided destruction of morphine salts.

The Extraction of Opium by Hot Water.—Our single experiment on this point illustrates once more what has been previously shown by others, *viz.*, that water alone does not completely extract morphine compounds from opium. In our sample we found 0.17 per cent. of morphine (nearly 2 per cent. of the total originally present) was not extracted even under somewhat drastic treatment. We also found that the destruction of morphine by prolonged digestion of the extract was 0.91 per cent. (more than 9 per cent. of the total originally present). While these points are not new, it appears to us that they call for more notice than they have yet obtained seeing that they have bearing both on some methods of assaying opium and on the preparation of certain pharmaceutical products.

This work was planned and carried out by us in the Analytical Laboratory of the Department of Customs and Inland Revenue, Ottawa, Canada. We wish to extend our thanks to Mr. F. W. Babington the head of that Laboratory for many acts of kindness which gave us time and opportunity to do more than the routine work which was necessarily our chief concern.

THE MULFORD BIOLOGICAL EXPLORATION OF THE AMAZON BASIN.

Preliminary and more or less erroneous announcements of this enterprise have appeared in the daily press, but without details as to the objects of the work and its special relations to medicine and pharmacy. The following is a complete prospectus of the Exploration.

The original idea of the expedition was far less comprehensive than that which now has developed. Doctor Rusby having gained information from travelers in northwestern Brazil of certain medicines in use by the natives which possessed very interesting properties, and properties that might render them of value in medicine, has long desired to observe their effects as there used, and to secure supplies for scientific investigation, and it was to carry out this object that the plan was originally conceived. In performing this work it would also be practicable to make a general collection of the flora of a very extensive region in southeastern Colombia and northwestern Brazil, in which no botanical collections have as yet been made. Since the New York Botanical Garden, Harvard

University and the National Museum have recently undertaken to prepare a flora of northern South America, including the region referred to, this added work would be most timely. Additional interest attached to such collecting because it would go far toward completing the survey of the Andean flora on which Dr. Rusby has done so much in his travels in Chile, Bolivia, Colombia, Brazil and Venezuela. Dr. Rusby is, moreover, Honorary Curator of the Economic Museum of the New York Botanical Garden, of which an elaborate catalogue is now going through the press. In the performance of this work he has been impressed with the long list of economic products of the region in question of which no authentic museum specimens exist. Many of the drugs of the region are very imperfectly known, as to their origin and collection. In the same connection, the Doctor was desirous of visiting southeastern Bolivia, the only part of that country where he has not made collections. With all these objects in view, Dr. Rusby appealed to the H. K. Mulford Company for coöperation in the carrying out of such an undertaking. Mr. Milton Campbell, the President, submitted the idea to his scientific department, with the result of considerably extending the scope of the work. It was pointed out that a number of the endemic diseases of the tropics were very imperfectly known, and that their careful study would not only prove of scientific value, but might result in the discovery of curative measures. It was particularly desirable that the transmission of diseases by insect agency should be thoroughly investigated. A discussion of these subjects showing that their investigation was feasible, the proposition was submitted to the Directors of the Mulford Company and was approved. Dr. Rusby's original plan, as submitted to Mr. Campbell, had included provisions for commercial adjuncts by which the expenses of the exploration would be repaid and a probable profit returned, but the Mulford Company deleted these items, stating that they preferred public recognition as making a contribution to science and to medicine, free from all direct commercial returns.

The subject of entomology having thus been included in the research, it was decided to broaden this work and to make a general collection of insects, and arrangements were made with the United States Bureau of Entomology to classify these insects and report upon them. Out of these discussions a suggestion arose for studying methods of repelling or destroying the numerous tropical insects which so annoy travelers and not infrequently become the indirect

causes of fatalities, and officers of the Federal Insecticide and Fungicide Board prepared a comprehensive series of formulae of substances that might prove useful in this direction. Supplies of these mixtures will be taken and systematically tested. At the same time, every opportunity will be improved for recording the pollination of flowers by particular insects and those destructive to timber and other vegetation will be studied It is hoped that the Bureau of Entomology may detail one of its representatives to accompany the party.

Dr. Rusby had been greatly interested, on previous expeditions, in the immense variety of fishes in the Amazon basin, and in the peculiar characters and habits of many of them, and determined to carry materials for extensive collections of this fauna. On submitting this idea to Drs. David Starr Jordan, and C. H. Eigenmann, among the leading authorities on the subject, they at once expressed their readiness to assist in the investigation of the fishes collected. It is also probable that they will be represented upon the Exploration by one of the ichthyologists from the University of Indiana.

Among other subjects of interest, is that of oil-seeds, of which there is a vast variety in the forests of tropical America. From fifty to a hundred pounds or more of each of these will be collected as encountered, and these will be shipped home for expression and the study of their oils. Professor Augustus A. Gill, of the Boston Institute of Technology has undertaken to pursue these researches. Similarly there are very many plants containing essential oils that are likely to prove of value, and Dr. Edward Kremers, of the University of Wisconsin will interest himself in the study of these. The region to be traversed abounds in serpents and other reptiles, both poisonous and innocent. These will be preserved like the fishes. The batrachians will be sent to Professor Ruthven, of the University of Michigan, and the others to the American Museum of Natural History in New York City.

While all these subjects are of great interest, the special work of Dr. Rusby and his party will be in connection with medicinal plants and drugs, for the study of which elaborate provisions have been made. Dr. Rusby hopes to shed fresh light on the manufacture of blow gun and other arrow poisons, of which several varieties appear to be in use in the region to be visited. Some of the more important commercial drugs will be traced to their origin, and absolutely authentic material will be secured for study. A very

superior quality of rubber is produced in the region and this will receive close attention. No opportunity will be lost for securing materials from which the nature of tropical diseases can be studied in the Mulford Laboratories at Glenolden.

The complete study of the medicinal products will occupy the attention of many specialists. Dr. Rusby will himself undertake their botanical classification and description. Their microscopical study will be pursued by Dr. Ballard at the Columbia University School of Pharmacy, by Professor Younken at Philadelphia, Schneider of Nebraska, Newcomb of Minnesota and others. Their chemistry will be studied by Arny of Columbia, Jordan of Purdue, Sayre and Havenhill of Kansas. The study of their physiological and medicinal properties will occupy the attention of many medical men at Yale, Harvard, the University of Pennsylvania, Johns Hopkins, and connected with the American Medical Association headquarters in Chicago.

The Division of Biology and Agriculture of the National Research Council has interested itself actively in this enterprise and has rendered valuable assistance.

The general route to be traversed by the party will be the country along the base of the Andes from Villavicensio, southeast of Bogota, to Calamar, several hundred miles south. At various points the valleys and canons issuing from the mountains will be ascended and collections made. A number of lakes along the route will also be visited. At Calamar, land travel will be abandoned and river-boats secured for the descent of the Uaupes River. Until a recent period, only the lower part of this river was known to science. There are a number of rubber collecting stations along its course, and it has been more or less traversed by traders. For the most part, however, this region is occupied by little or not at all civilized aborigines, who at times at least have exhibited hostility against the whites. For our knowledge of this region, science is almost wholly indebted to the work of Dr. Hamilton Rice, who, in the face of great difficulties, and under great hardships, traversed the river almost from its source to its mouth at the Rio Negro. Dr. Rice has gienn us two excellent and comprehensive accounts of it, in the *Geographical Journal* for June, 1910 and August, 1914. Both papers are accompanied by maps, not only of this, but of neighboring rivers which he first explored.

Judged by its peculiar position and topography, the section to

be studied must be very rich in its variety of both plants and animals. It is probable, moreover, that its paleontological records are of great interest. Into this field of collection, however, the party cannot enter, because of the time required for the collection of fossils and the weight of the specimens.

On reaching the Rio Negro, the party will descend to its mouth at the Amazon, which they expect to reach early in July, thus avoiding the rainy season north of the Amazon. At this time the dry season will begin south of the Amazon, and the party will then commence the ascent of the Madeira, the largest southern tributary of the Amazon. Steamers run direct from Manaos on the Amazon, to the lowest cataract of the Madeira. From there a railroad runs to a point above the highest fall, where small steamers ply to points well toward the sources of the Madre de Dios, Beni and Mamore, tributaries of the Madeira. Various points on all of these streams will be visited, according to the time available, and the party will then proceed by canoe or raft as far into the eastern Andes as possible, later crossing the mountains by mule-train and emerging via La Paz, at one of the Pacific ports. Should time suffice, a stop will be made on the return journey for an incursion into Colombia on the west side of the mountains, where some important drugs are to be found.

During about six months of the year that the exploration is expected to occupy, the party will be entirely isolated from civilized sources of support, and dependent on their own resources. Since the country abounds in fish and game, and since many sources of food-supply in the form of wild vegetation are known to Dr. Rusby, it would be possible to subsist largely on the natural food supplies of the country. The obtaining of such supplies, however, would consume much precious time that would otherwise be devoted to scientific collection and recording. For this reason, a food supply sufficient for the entire time will be carried into the wilderness. These supplies have been carefully selected, so as to provide a daily ration that is both wholesome and agreeable, since Dr. Rusby has learned by experience that many, if not most, of the ills from which such travelers suffer have their basis in poor nutrition. An ample supply of medicines will also be taken. Since one does not know what particular medicine may be needed, a full supply must be made available. Quinine, in the form of the bimuriate, will of course, be the principal item in this line. The onset of malarial fever may

be said to be impossible when the blood contains a sufficient amount of this alkaloid.

A full outfit of tents, cots, hammocks, bedding, canopies and camp equipment has been carefully selected. A large part of the stores have been purchased from the surplus stock of the U. S. Army.

It was originally designed to carry several of the folding canvas boats manufactured in Kalamazoo, but inquiry has developed the advice that these boats could not stand the rough waters to be navigated. The native river boats are very heavy, with thick and hard walls and can well resist the severe shocks resulting from striking upon the rocks in the rapids. At many points, of course, the boats must be taken out and portages made.

The party will of necessity be well armed, primarily in order to be able to secure such game as comes within reach, but also to guard against possible native hostility. Every precaution will be taken to avoid such encounters, and one of the surest ways of accomplishing this object is that of presenting a strong defensive position.

Among the drugs which it is expected will be encountered are tolu, ipecac of both species, simaruba, guaiac, copaiba of several species, manaca, guarana, muira-puama, caroba, several resins, coto and para-coto and cocillana.

LAW-MAKING, RATIONAL AND IRRATIONAL.*

By James H. Beal,

Urbana, Ill.

The faith of the average American citizen in the all sufficiency of legislation to cure social, economic and moral evils is child-like and bland—a faith that is never chilled by the fact that rarely in his experience has he known a law to accomplish more than a fraction of the good that was predicted of it, and that many laws have either failed altogether or have introduced greater or more numerous evils than those they were intended to cure.

The framers of the American system of government proceeded upon the theory that the people who were least governed—who had the fewest laws to obey—were the best governed. To-day this ancient and once honorable doctrine is very much in the discard.

* Address delivered to Urbana Association of Commerce. Reprinted from the *Urbana Daily Courier.*

No matter what evil is under consideration, the first remedy thought of or proposed is legislation. The new bills introduced during the life of a single congress may run into the tens of thousands, and even a state general assembly may be called upon to consider more than a thousand proposed new laws during a single session.

Granting that our highly organized civilization, with predominating industrial and commercial interests, may require a more complex system of jurisprudence than would serve the necessities of a less specialized social organization, it is entirely absurd to assume that society needs the amount of regulation that these frantic attempts at law making would indicate. Comparatively few of the proposed new laws possess any real merit. A large proportion simply reflect the spirit of meddlesomeness that governs the minds of those who gratuitously assume both their right and their ability to prescribe the standards according to which their fellow citizens shall order their morals, their occupations and their daily lives.

Assuming that we shall continue to grind out national and state legislation at the present rate, what will be the volume of written law in another twenty-five years?

Consider also the bulk of secondary legislation in the form of rules and regulations adopted by the administrative officers of the law. Congress adopts a measure covering four or five pages, whereupon the department of administration issues a code of regulations covering fifty or sixty pages, introducing obligations and producing results which the original law making body could not have contemplated.

This country began its existence with the freest government on the face of the earth, and under the freest of governments our people have prospered as no people ever prospered before. Unless the present craze for law making can be checked, the next generation will find itself subject to more regulation than was old verboten-ridden Germany, and under the rule of more bureaus and bureaucrats than Russia under the czars.

THE INABILITY OF REFORMERS TO LEARN FROM EXPERIENCE.

Somehow men do not seem to learn, or at least do not heed, the lessons of experience in politics as they do the lessons of physical science.

In the physical sciences facts ascertained by careful experimentation are recorded in literature and become a part of the general in-

heritance of the race, so that men do not waste their lives in forever trying out the things that have been fully tested previously.

In political science, however, we do not seem to be able to record well established political and economic facts in such a way as to impress them upon the popular mind and save the world from endlessly trying over and over the same old experiments that have been tried and have failed numberless times before. These facts have been recorded, however, and are available to those who will take trouble to look for them.

SUCCESSFUL LAWS MARK REFORMS BUT DO NOT MAKE THEM.

One of the facts we may learn from the history or political experiments is that successful laws do not make reforms, but only mark them, that is, they mark the periods when the reforms have so far gained the consent of the minds and hearts of the people that the written statutes are merely concrete expressions of the will of a liberal majority of those who are to live under them.

If a proposed reform will really make the world a better place to live in, it is necessary only to convince a majority of the people of its wisdom and desirability when appropriate legislation will follow logically and naturally. Generally, however, the radical reformer resents the slow and cumbrous methods of education and prefers to make an organized assault upon the law making body and compel an immediate acceptance of his alleged reform by act of legislature.

When the premature law is openly derided and violated with comparative impunity, the reformer will not admit, and probably does not realize that the legislation was in advance of genuine public sentiment. His remedy is to adopt still more legislation of the same kind, piling prohibition upon prohibition and penalty upon penalty, with the result of producing an ever increasing number of violations, and a diminished respect for the law.

If mere law making could make men or society perfect, the world would have been free of evil millenniums ago. Every known political and social tort has been legislated against thousands of times and yet these wrongs persist, and not a few when traced to their sources will be found to be the direct outgrowth of the very laws intended to prevent them.

REFORM LEGISLATION IMPOSES BURDENS UPON INNOCENT PEOPLE.

Another fact to be learned from the history of experiments in law

making is that reform measures invariably impose burdens upon perfectly innocent people who do not stand in need of reformation and invariably place restrictions upon acts that may be wholly without evil or even meritorious.

This has been true of every piece of reform legislation that has ever been placed upon the statute books. The best of reform measures are mixtures of good and evil, and not a few alleged reform measures have been responsible for the growth of greater evils than those they were intended to cure.

Common sense therefore demands that we take into consideration the burdens a proposed law will certainly impose upon innocent people and upon innocent industries as well as the good results which it is hoped the law will produce. Like other things, a reform law may some times cost more than it is worth.

The exact point at which the evils of a reformatory law begin to outweigh the good cannot be determined with certainty in advance of actual trial, but experience teaches that it usually falls short of the extreme limit which the radical reformer is inclined to demand.

EXCESSIVE REGULATION PRECEDES THE DESTRUCTION OF LIBERTY.

Another fact constantly brought to the attention of the student of political history is that peoples who have obtained their liberties by the most heroic of sacrifices have so frequently thrown them away again in the frivolous pursuit of things they thought would make their liberties still more secure and their freedom still more free.

The story of the democracies that have failed shows that their vigor and prosperity regularly declined with the growth of internal legislation, or with the forcing of obnoxious regulations upon their citizens by the factions which successively obtained control, until they had so weakened themselves by internal strife that they fell to pieces of their own weight or were an easy prey to enemies from without.

Of course, no people ever intentionally destroyed their own liberties. They always intended their law making to make their countries better and stronger. Their uniform mistake was in consenting to the violation of fundamental principles for the sake of some fancied immediate good which their radical legislation was expected to accomplish.

The one great lesson of all these unsuccessful attempts at self-

government is that a nation which willingly submits to the suspension of the principles of free government for the sake of expediency, or for the accomplishment of some quick and immediate reform will in the end always come to grief. Principles that can be suspended for beneficient purposes can also be suspended for evil purposes, and laws intended for purely good ends can also be enforced oppressively.

THE FUNDAMENTAL PRINCIPLES OF FREE GOVERNMENT ARE PERMANENT.

Another lesson from the history of political experiments is that the fundamental principles of free government do not vary with the changing values of the factors of civilization. A principle of government essential to the preservation of liberty in one age is essential to the preservation of liberty in every age.

By certain doctrinaire reformers of the present day the United States constitution is considered to be obsolete and out of date because it was composed before the age of telephones, wireless telegraphy and flying machines. It would be as reasonable to consider the principles of arithmetic as obsolete because they were discovered before the invention of modern business methods.

Civil government is not a problem of mechanics but of human nature, and no group of men who ever lived had a keener or closer information of the essential qualities of human nature than the statesmen who formulated the federal constitution and the bill of rights that was made a part of that document. They were not only men of rare natural ability but they met their task, with a face to face directness and with a freshness of experience with governmental tyranny that their successors have not had.

These men said: No government has ever had unlimited power over the lives and destinies of its people that it did not eventually exercise its powers oppressively. We will prevent such a disaster by making it a fundamental principle of the federal constitution that the powers of the government shall be limited strictly to matters of general concern, and will prohibit its interference in the lives and liberties of the individual citizen, except in so far as they are intimately and directly connected with the powers expressly given. Similar considerations induced the placing of corresponding limitations upon the powers of the governments created by the earlier state constitutions.

The doctrinaires are now ready to tear these old and well tried charters of liberty to pieces and to confer upon the legislative and executive departments the very powers which the elder group of statesmen were certain should be withheld from them. Perhaps the doctrinaires are right; but if our government can possess unlimited powers without using them oppressively, it will be the first instance of its kind in all the history of civilization.

NO LAW CAN BE 100 PER CENT. EFFICENT.

Another lesson of political history is that even the best of laws will fall far short of complete efficiency in removing the evils at which it is aimed. Whether we have one law or a thousand upon a given subject, there will always be a residium of evil that mere law making will not cure. When this irreducible minimum has been reached the multiplying of prohibitions only multiplies the number of violations.

It is an accepted principle in mechanics that no machine can be expected to reach 100 per cent. in practical efficiency, and the mechanician therefore directs his efforts to obtaining the most profitable ratio of power expended to work delivered. Strangely enough, people who do not expect to obtain one hundred per cent. efficiency from any construction of wood or metal, are forever trying to compose laws that shall be one hundred per cent. efficient, that is to say, laws that cannot be or that will not be violated.

Some thousands of years ago there was promulgated a code of ten commandments governing the fundamentals of social and moral conduct, and in all the centuries since then the divine author of that code has neither repealed nor amended a single one of the ten original articles. A divine intelligence could be expected to understand that if men are disposed to disobey the commandments of a primary code they will be equally disposed to disobey the provisions of all subsidiary codes of amendments and regulations, but human law makers, when they discover that one set of statutes is being violated, seem to imagine that by the adoption of a new code of regulations, or by rearranging the phraseology of the old code, the law violator will become a law observer.

The law making bodies of this year are busy amending and reforming the laws adopted at previous sessions. Last year they were doing the same thing. Next year they will be repeating the process.

Each successive measure in its day was proposed as an important and necessary reform, and those who dared to oppose it were denounced as reactionaries and obstructionists, or worse. When in time its defects became evident, it was then attacked as an abuse by a new set of law makers, the successive crops of reformers jumping over each other's heads like a group of boys at leap-frog.

What we all must learn is that the best possible law will fall considerably short of perfection, and that when any comprehensive and well considered law has once been placed upon the statute books our attention should be given to its enforcement, and not wasted in impossible attempts to devise measures that cannot be violated.

EXCESSIVE AND RADICAL LEGISLATION PRODUCTIVE OF LAWLESSNESS.

Another lesson of political history that many reformers have failed to learn is that excessive and extreme legislation is of itself a most potent breeder of lawlessness.

Every student of history knows that, without exception, periods of excessive and radical regulation have always been followed by periods of equally extreme and radical reaction.

Seemingly there is a certain ration or balance of regulation that must be maintained to obtain the best results for law and order. Human nature will stand for coercion without reaction up to a certain limit, but if this limit be exceeded there will be a moral break down that makes the individual less amenable to the reasonable restraints of the law than before.

The very extremity of a law may constitute the most potent reason for its violation. In other words, the profits of violating the law may be so great, and the risk of punishment so small in comparison that the hazard is really not much greater than the hazard of lawful occupations that are much less profitable. Such laws in effect place a premium upon law breaking, and penalize the law-abiding. Citizens who are naturally inclined to obey the law find themselves at a disadvantage as compared to those who ignore it, and there is a letting down of moral tone all along the line.

Most men believe that the chief function of government is to protect them from oppression. When the citizen comes to feel that the government itself has become an oppressor he is already at heart a potential law breaker, ready to evade the mandates of the law whenever he thinks it safe to do so.

THE FAILURE OF EMOTIONAL LEGISLATION.

That some laws succeed fairly well in correcting the evils at which they are aimed all can testify from personal observation, that some laws do not work at all, or have a back action that is worse than inaction, is a matter of common knowledge.

If we examine into a law that is known to work fairly well in practice we shall usually find it to be one that is not extreme in its provisions, and one that was formulated by cool and deliberate judgment in the light of well established precedents. If we examine into the laws that are admitted failures we shall find almost universally that they are extremely drastic in their provisions, that they were composed under the influence of strong emotions and passed under the whip of intensive propaganda.

When our emotions are aroused in public affairs we want direct action and lots of it, and we mistrust the motives of those who urge less drastic measures as a more certain, though slower and less spectacular method of reaching the desired end.

We regulated the railroads with our emotions instead of with reason and judgment until we regulated them nearly into bankruptcy. Now at tremendous cost we are painfully trying to work back to the line of reason and moderation.

When we undertook to regulate the trusts we again rejected the teachings of experience and the reasonable judgment of experts and followed emotional leadership with the result that we hobbled and altered legitimate business enterprises without materially curbing the operations of those the law was intended to reach. This emotionally formulated law has not only operated to prevent small business men from combining to protect themselves from the aggressions of large capital interests, but every time Congress has passed an appropriation bill it has been reduced to the pitiful expedient of expressly providing that the money appropriated shall not be used to prosecute violations of the law by certain strongly organized interests.

Why is it that we have so frequently followed emotional leaders and rejected the counsel of conservative statesmanship? Simply because of our impatience for immediate results. It is the same disposition that prompts the teacher or doctor or merchant to withdraw his small hoard from the security of the savings bank and invest it in oil stock that promises a thousand per cent. return.

Common horse sense, or even average mule intelligence should teach us that in political affairs as in business enterprises the more profuse the promises the less likely the performance. The promotor of "get-rich-quick" concerns can always promise greater returns on the investment than can be offered by the promoters of legitimate business undertakings.

LAWS FAIL WHEN THEY IGNORE HUMAN NATURE.

Another lesson from the history of political experiments is that laws also fail when they ignore the ordinary qualities of human nature instead of operating in harmony therewith.

The engineer who digs a tunnel, or drains a swamp, or irrigates a desert, does not begin operations without a careful and scientific study of all the surrounding conditions. Sometimes he finds a direct method of approach the most suitable, sometimes an indirect approach, and his success is measured by his ability to adjust his methods to the peculiar circumstances in each case. Sentiment and emotion find no place in his plans. He does not attempt to destroy the natural tendency of water to flow down hill, but makes use of a fall of water at one place to carry water up hill at some other place. He does not ignore or attempt to violently suspend the operation of natural laws, but seeks to utilize them in the attainment of his purpose.

The reformer of political and social institutions, in his anxiety for direct and immediate results, rarely takes time to patiently study the particular conditions involved, refuses to be bound by the laws of human nature, and will not consider any other method of approach than the age-old formula, "it is forbidden," which in the history of civilization has failed as often, if not oftener, than it has succeeded.

Some evils of the body politic are of such a nature that the only proper course of procedure is to totally prohibit them, but others are like the tares in the wheat that cannot be directly uprooted without uprooting the wheat also.

Human nature in the mass can be led by education and persuasion, it cannot be successfully driven. Laws that are passed by tricky political methods or adopted with the grudging assent of a bare majority, and which attempt to violently uproot world-old prejudices or beliefs in a day retard rather than advance genuine reform.

WE TALK EUGENICS AND PRACTICE ANTI-EUGENICS.

One who should study the accomplished and attempted legislation of the last quarter of a century might reasonably arrive at the conclusion that the chief object of civil government is to protect the mentally incompetent, the morally weak or vicious and the physically unfit. He would observe, for example, that the law makes it difficult to secure useful and necessary drugs for the treatment of the mentally and morally competent in order to keep them out of the hands of degenerates who might use them to their own hurt. He would discover legislation to handicap the enterprising and progressive business man in order to enable the less enterprising and less progressive to succeed. He would note the legislation of trade union rules designed to penalize the skilled and industrious artisan and prohibit him from producing more or better work than the unskilled and lazy. He would discover numberless schemes, either accomplished or in process of accomplishment, designed to pension the lazy, incompetent and wasteful members of society and to collect the pensions from the industrious, competent and economical members. He would observe parlor philosophers talking about the importance of developing a mentally fit and physically strong and virile race and advocating governmental and social policies designed to produce the opposite.

Since we have such an abundance of societies and devices intended to favor and protect weaklings and degenerates, would it not be timely for humane people to establish a society to protect the rights of those who are neither weak nor vicious, who exercise a proper restraint upon their appetites and passions, who are industrious and thrifty, and in every way prove their right to respectful consideration?

Is it not time to return to the viewpoint of the fathers of the republic as to the proper functions of government, and to realize that the sane and decent members of society possess certain inalienable rights of which they should not be deprived in order to confer special benefits upon those who do not deserve, or who have abused the privileges of citizenship?

No good citizen would willingly oppose any sane attempt to reform whatever may be amiss in our social or political institutions, but surely we are entitled to demand that such reforms be framed with due regard for the rights of the innocent bystander.

STANDARDIZATION OF TINCTURE OF STROPHANTHUS.*

By C. T. Bennett, B.Sc., F.I.C., F.C.S., Pharmaceutical Chemist.

Without attempting to carry out the elaborate researches suggested in the Conference Research List, I venture to put forward a few suggestions for the consideration of a future Pharmacopoeia Revision Committee.

The variation in strength of tincture of strophanthus was the subject of a note by my late chief, Mr. J. C. Umney, published in *The British and Colonial Pharmacist* of December, 1918, p. 375. In this note it was pointed out that the standards adopted for physiologically testing this potent drug differed considerably, the minimum lethal dose calculated for a 100 Gm. frog being as follows for various commercial samples:

	M.L.D. for 100 Gm. Frog.
U. S. P. standard (1 hour).....	0.006 Cc.
Standard adopted by the Society of Apothecaries.....	0.020 (since altered to 0.01 Cc.)
Sample "A" (time not stated).....	0.007 Cc.
Sample "B" (time not stated).....	0.020 Cc.
Sample "C" (time not stated).....	0.050 Cc.
Sample "D" (2 hours).....	0.150 Cc.
Sample "E" (2 hours).....	0.150 Cc.

If the standards adopted vary to such an enormous extent as shown by these figures, then it is obvious that physiological standardization will fall into disfavor unless an international standard be agreed upon.

According to Rowe (*Y. B. P.*, 1917, p. 264), commercial samples of strophanthus tested physiologically have shown enormous variation in potency, but since 1913 samples examined by him have been much more uniform. He takes exception, however, to the use of ouabain or gratus-strophanthin as a standard, and considers that crystalline Kombé strophanthin is the proper standard.

The strength of the tincture official in the British Pharmacopoeia, 1914, is four times that of the 1898 tincture, *viz.*, 1 in 10 by volume (100 Gms. of the seeds in 1000 Cc. of tincture) in accordance with the International Agreement of 1906, and identical in strength with that of the United States Pharmacopoeia, except that the latter is prepared with 95 per cent. alcohol.

* Reprinted from *The Pharmaceutical Journal and Pharmacist*, July 24, 1920.

The questions to be considered are as follows:

1. Is strophanthus of sufficient importance to the medical profession to warrant a thorough investigation of the glucosides found in the various species?

In reply to this I can only repeat Mr. Umney's statement that tincture of strophanthus is rapidly going out of use owing to its variable strength and the uncertainty of its results.

2. As at the time of writing it is impossible to obtain unmixed seeds of *Strophanthus Kombé* (which are alone official in the British Pharmacopoeia) in sufficient quantity to meet the demand, which variety would be the best substitute? This question can only be answered by a more thorough investigation of the various species.

3. Is it practicable for the collection of the most suitable variety to be under the supervision of a competent botanist? It should be possible for the importers to make some arrangements for this, even if higher prices had to be paid for the seeds.

4. Could the glucoside strophanthin, which is official in the United States Pharmacopoeia and in the French Codex, or a preparation of it, be employed to replace the tincture in pharmacy? If the glucoside, or mixture of glucosides obtained from a definite species were made official, then it would be desirable to describe its characters in order to ensure the purity of the product and uniformity of medicinal action. Unfortunately, the chemical and physical characters of the various glucosides found in the different species are not sufficiently known for the fixing of a definite standard.

I do not propose to burden this note by summarizing the researches carried out by various workers on the glucosides found in the different species, especially as the results are considerably at variance, but I would like to point out that no definite standard is laid down by the U. S. P. monograph for strophanthin, while the French Codex gives a melting point of 185° for strophanthin obtained from *Strophanthus hispidus*. According to Cohen (*Y. B. P.*, 1913, p. 134) *h*-Strophanthin from *S. hispidus* sinters at 160°, but does not melt at 190°, *g*-Strophanthin from *S. gratus* sinters at 185°, and *k*-Strophanthin from *S. Kombé* sinters at 170°.

5. If physiological standardization is to be adopted, what is the best method of procedure?

Possibly an agreement could be arrived at between the respective Revision Committees of the British and United States Pharmacopoeias. The chief objection to physiological standardization is that

the action on a frog may be very different from that on a human being. In physiological tests no attention is paid to the age of the frog.

6. If physiological tests are not thought desirable, is a chemical method necessary and practicable? Although the chemical methods which have been proposed have some disadvantages, it seems desirable that a standard for the seeds should be fixed by the British Pharmacopoeia, as this procedure would at least ensure an approximately uniform tincture.

The standardization of strophanthus must, therefore, be undertaken either by the botanist, the physiologist, or the chemist, or preferably by the coöperation of all three, if we are to ensure uniformity of strength. As a chemist, I am strongly in favor of chemical assay, and a review of the processes has led to the conclusion that Barclay's method as modified by Haycock is the most suitable for general adoption. (See *Y. B. P.*, 1911, p. 125.) The standard I would suggest for the seeds is 6 per cent. to 8 per cent. of strophanthin or 0.6 per cent. for the tincture.

COLOR TEST FOR OXALIC ACID.*

By Lewis H. Cheinoff

DENVER, COLO.

A few crystals of resorcinol are added to about 5 Cc. of the unknown solution in a test-tube, and the mixture is warmed slightly to dissolve the resorcinol. It is then cooled and 5 Cc. of conc. sulphuric acid is carefully and slowly poured in along the side of the tube so as to form a layer. A blue ring will be formed at the junction of the 2 layers, if oxalic acid is present. The color is best seen if held to the light in front of a sheet of white paper. Care must be taken that the mixture does not warm up appreciably. If the blue color does not appear in a few minutes, the mixture is shaken thoroughly, and, after cooling somewhat, 5 Cc. more of sulphuric acid is added. Should the color still fail to appear, the mixed contents of the tube should be gently warmed over a flame (not boiled) when an indigo blue color will diffuse throughout the liquid. If the mixture be cooled with ice-water, the color will disappear only to

**Journal Amer. Chem. Soc.*, Sept.

reappear again on heating. If the mixture be boiled a few minutes, the color will turn a deep dark *green*, which will become a light yellow-green on cooling. If to the cold yellow-green solution an equal volume of sulphuric acid be added so as to form 2 layers, the *blue* color will again appear. It is believed that all these reactions taken together are characteristic of oxalic acid alone.

This test may be made sensitive to one milligram if the dry unknown substance be warmed with 2 drops of a 10 per cent. aqueous resorcinol solution and the sulphuric acid added drop by drop. The blue color then appears immediately. For very dilute solutions of oxalic acid or its salts, it is best to evaporate to a concentration of about 10 per cent.

If interfering substances are present the oxalic acid may be precipitated in ammoniacal solution as the calcium salt, washed with water, and the test applied directly to an aqueous suspension of the salt.

CURRENT LITERATURE.

TRADE INTEREST.

ALSATIAN POTASH.—The French Minister of Agriculture, in a notice published in the *Journée Industrielle*, reminds persons interested in the purchase of Alsatian potash salts, that trade in this commodity is now free. He adds that orders for potash are no concern of his Department, and that they should be sent either to Mulhouse, or to the various representatives of the Société Commerciale des Potasses d'Alsace. Whereas before the war the consumption of pure potash in France did not exceed 37,000 tons a year, the mines of Alsace were able to send to France no less than 47,000 tons of pure potash in the year 1919, and 30,000 tons in the first half of the present year. Many orders which were given sometime ago have not yet been delivered, but the Minister of Agriculture has been able to arrange that a sufficient number of trains shall be placed at the disposal of the mines, to insure the delivery of 5,000 to 8,000 tons of pure potash a month. It is, therefore, to be presumed that delays in delivery will no longer occur. (From *The Pharm. Jour. & Pharm.*, Sept. 4, 1920.)

MEDICAL AND PHARMACEUTICAL NOTES.

THE CLINICAL SIGNIFICANCE OF CYLINDROIDS.—On the basis of examination of 81 cases of uncompensated heart disease, Eigenberger reports that his results confirm the views of von Jaksch and Quensel, who ascribe to cylindroids a certain clinical importance as signs of disturbance of renal circulation. Eigenberger could demonstrate cylindroids in 36, or 44 per cent., of his 81 cases. In most of the cases in which cylindroids were present there were strong clinical signs of disturbed renal circulation. In 2 of the cases with large number of cylindroids, necropsy disclosed marked renal stasis. (From *Zentralblatt für innere Medizin, Leipzig*, May 15, 1920, 41, No. 20; through *Jour. Amer. Med. Assoc.*, August 28, 1920.)

BETTER WAY TO GIVE BENZYL BENZOATE.—To overcome the unpleasant, bitter, burning taste of the alcoholic solution of benzyl benzoate Hirschfelder gives pure benzyl benzoate, 10 parts; emulsion of acacia, 5 parts; elixir eriodictyon aromaticum (N. F.), 35 parts; dose, one teaspoonful. He has been able to secure relief of symptoms in a considerable number of cases of conditions caused by spasm of smooth muscle, cardio-spasm, pylorospasm; pain in gastric ulcer from aspastic constipation. The relief occurs within half an hour after taking and lasts. Benzyl benzoate brings about relief in many, but by no means all, cases of bronchial asthma, just as is true of atropine or other drugs that inhibit the vagus. Still more striking results have been obtained in the treatment of dysmenorrhea. About 80 per cent. of the patients have had relief from pain after from one to three doses. (From *Minnesota Medicine, St. Paul*, August, 1920, 3, No. 8; through *Jour. Amer. Med. Assoc.*, August 28, 1920.)

VALUE OF COLLOIDAL GOLD TEST.—The results of other workers regarding the value of the colloidal gold test in the diagnosis of general paralysis are confirmed by Cruickshank. The substance in the spinal fluid of general paralytics which causes precipitation of colloidal gold is not dialyzable and resides in the globulin fraction of the protein and in this respect resembles the Wassermann reacting substance. It is not altered by heating to the coagulation point of protein. The reaction is not due to peptone. The various types of reaction can be simulated by mixtures of globulin and albumin, the globulin acting as a precipitating agent and the albumin

as an inhibitory or protective one. Syphilitic reactions are due to an amount of albumin sufficient to obscure partially the precipitating effect of the globulin. As the globulins obtained from negative spinal fluids, even when used in concentrated form, are almost inactive, the precipitating action of paretic fluids cannot be ascribed solely to the increase in globulin, but is probably dependent on a specific alteration of the physical state of the globulin, which is associated with a positive electric charge. Human serum globulin has the characters of a positive colloid, but the paretic and syphilitic reactions of spinal fluids cannot be attributed merely to the passage of serum globulin into the spinal fluid. The meningitic reactions, on the other hand, may be due to the leakage of plasma through damaged meninges. (From *British Jour. of Exper. Pathology, London*, April, 1920, 1, No. 2; through *Jour. Amer. Med. Assoc.*, August 28, 1920.)

BENZYL BENZOATE IN WHOOPING COUGH.—The number of cases studied by Macht was about 115. All these cases were characterized by whooping and in many the paroxysms were accompanied by vomiting and small hemorrhages. Most of the patients before coming under Macht's observation had been treated by parents or doctors with paregoric and other popular drugs without any benefit, while others had been left alone without any treatment whatever. A number of the patients received vaccine treatment, but the results in these cases were also not at all striking. All other medication was discontinued and the patients were given a 20 per cent. solution of benzyl benzoate by mouth. The dosage varied from 5 to 40 drops in water three or four times a day and oftener, depending on the age of the patient and the severity of the disease. In cases in which the simple alcoholic solution of benzoate was found to be too distasteful to the young patients it was flavored with a few drops of benzaldehyde and the medicine was administered in sugar, water or milk. The addition of a little benzaldehyde to a solution of benzyl benzoate in amounts varying from 1 to 5 per cent. produced a mixture which seemed to act more effectively in cases of whooping cough than benzyl benzoate alone. It was found that the administration of benzyl benzoate in the form of a suspension in simple elixir, in syrup of yerba santa and other syrups or elixirs was not a satisfactory method either of disguising the taste or administering the drug over long periods of time. About

90 per cent. of all the patients showed more or less beneficial effects; about 50 per cent. exhibited marked improvements in the symptoms. The therapeutic effects of benzyl benzoate were not of a curative character but were of a distinctly palliative nature. (From *Bull. of Johns Hopkins Hospital*, Baltimore, 12: No. 4 (July), 1920; through *Jour. Amer. Med. Assoc.*, August 28, 1920.)

BENZYL BENZOATE FOR PERSISTENT HICCOUGH.—The value of the new antispasmodic benzyl benzoate has lately been demonstrated in the treatment of persistent hiccough. Three cases are recorded which were eased by the drug in a very short time, all of which had resisted ordinary treatment. One case was cured by the administration of one dose of 25 drops of a 20 per cent. solution in alcohol, equivalent to 5 minims of benzyl benzoate. It is suggested that the drug should prove of diagnostic value in differentiating hiccough of purely central origin from that of peripheral origin. As the chief effect is on smooth muscle, it should prove useful for the relief of the latter. Benzyl benzoate is best administered in the form originally suggested by the author, namely a 20 per cent. solution in alcohol. Of this solution the patient takes 20 to 40 minims in water or milk. It is neither convenient nor advantageous to give the drug in suspension in syrups or elixirs; and the administration in capsules has produced irritation in some cases and rendered the therapeutic action too slow in others. To children the solution can be conveniently given in sugar, water or milk. (*Med. Record; Lancet*, 199, 512, 1920; through *Pharm. Jour & Pharmacist*, September 11, 1920.)

INFUSION OF PARSLEY FOR GALL STONES.—Attention is drawn by H. C. Kidd (*B. M. J.*, Aug. 14, 1920, p. 244) to the use of infusion of parsley in the treatment of gall stones. A lady over 70 years of age had suffered for many years from this trouble, with severe colic and jaundice. In November, 1918, she had a prolonged attack, which reduced her to the lowest extremity. In the region of the gall bladder was a large palpable mass in which gall stones could be felt. She was advised to undergo an operation but refused; and, having heard of a friend who had been cured by drinking infusion of parsley, she gave this remedy a trial. A double handful of fresh parsley leaves was soaked in cold water, which was afterwards brought to the boil, strained, and allowed to cool. She took a pint and a half daily of this infusion and in time this seemed

to cure her. She is now free from pain and sickness; the mass felt in the gall bladder has disappeared, and her general condition is satisfactory.

Dr. Kidd seems to have been unable to trace any reference in the literature to the use of parsley for this purpose, but we would point out that "compound mixture of agrimony," of which parsley is an important ingredient, has been in use in the north for many years as a remedy for gall stones. This mixture is an infusion containing parsley, barberry, agrimony, toad-flax (*antirrhinum*), taraxacum, caraway, chamomile, and rhubarb, the doses being half an ounce thrice daily. (From *The Prescriber*, October, 1920.)

EMETINE BISMUTH IODIDE: A NEW VEHICLE.—The difficulty of administration of emetine bismuth iodide has always been the fact that a portion of the drug is dissolved in the stomach, with resulting nausea. T. J. G. Mayer (*J. Trop. Med.*, May 1, 1920) claims to have found a vehicle that will carry the drug safely through the stomach. The drug is rubbed up with 16 parts of mutton fat, the mass moulded into rounded pills weighing about 7 grains, and each pill covered with a layer of mutton fat, applied with a paint brush. The mutton fat being solid at body temperature is not digested until it is too far beyond the pyloric orifice to be regurgitated and cause vomiting or even nausea. Pills containing one and one-half grains of the drug and about seven and one-half grains of mutton fat are about as large as may be conveniently swallowed. (From *The Prescriber*, October, 1920.)

MONARSONE: A NEW ANTISYPHILITIC.—A new arsenical compound for the treatment of syphilis is described by B. L. Wright *et al* (*Med. Record*, April 10, 1920). The substance in question is disodium monoethylarsone, $CH_3CH_2AsO(NaO)_2$, which for brevity they call *monarsone*. It contains 7 per cent. more arsenic than arsenobenzol; is decidedly less toxic than the arsenobenzol compounds; is perfectly soluble in small quantities of water, and may be given without danger in solutions containing 0.2 Gm. per Cc. Monarsone has no haemolytic action on the red corpuscles, and may be given intravenously without fear of extravasation, as leakage causes no untoward effect. It requires no special apparatus for its administration, and its solutions are so stable that they resist oxidation or decomposition when boiled or subjected to the higher temperatures of the autoclave. (From *The Prescriber*, October, 1920.)

RAPID PREPARATION OF MERCURIAL OINTMENT.—The addition of lanoline to the lard in which mercury is to be divided in making mercury ointment is one of the most efficacious methods of overcoming the difficulties encountered in incorporating the mercury. Considering that the action of the lanoline is due to its content of cholesterin, Dr. G. Fontes has experimented with the addition of that substance to lard with and without the subsequent admixture of water and reports the following results:

100 Gms. lard, with 2.5% cholesterin immediately absorbed 490 Gms. mercury.

100 Gms. lard, with 2.5% cholesterin and 20 Gms. of water absorbed 575 Gms. mercury.

100 Gms. lard, with 2.5% cholesterin and 50 Gms. of water absorbed 970 Gms. mercury.

100 Gms. lard, with 5% cholesterin absorbed immediately, 1,500 Gms. mercury.

100 Gms. lard, with 5% cholesterin and 100 Gms. of water absorbed 1,900 Gms. mercury.

100 Gms. lard, with 5% cholesterin and 160 Gms. of water absorbed 3,000 Gms. mercury.

The lard and cholesterin were melted together, the water was then incorporated and to the mixture the mercury was added in small portions stirring with a pestle. The metal was rapidly incorporated (extinction parfait). Ten minutes trituration sufficed to make the ointment. The product may be readily diluted with a fatty material or with petrolatum. (*J. Pharm. Chim.*, 1920, p. 195.)

J. F. C.

BENZYL BENZOATE IN HICCUP.—Macht has found benzyl benzoate to be an invaluable medicine in the treatment of persistent hiccup of both adults and children. Not only has it been found useful in allaying the ordinary mild forms of hiccup so common in infants, but the drug has been found to be efficient in stopping those forms of hiccup termed pernicious, that is, those cases in which the phenomenon persisted for long periods of time, from twenty-four hours to several days, and in which the singultus was unaffected by all other forms of medicinal treatment, both external and internal. Macht believes that benzyl benzoate also is of diagnostic value in differentiating between the hiccups of a purely central origin, on the one hand, and those which are due to some peripheral origin, on the other. In as much as benzyl benzoate exerts its chief effect peripherally on the smooth muscle structures, the author is inclined to

believe that this drug may be most useful in the treatment of hiccups of peripheral origin. The benzyl benzoate exerts its action best when given in a 20 per cent. solution in alcohol. Of this solution the patient is directed to take from 20 to 40 drops in water or milk. The author has not found it either convenient or advantageous to administer the drug in suspension in various elixirs or syrups, and administration in capsules has been found by him in some cases to produce local irritation, and in others to render the therapeutic action too slow. To children the solution can be conveniently administered in sugar, water or milk. (From *Medical Record*, New York, Jul. 24, 1920, 98, No. 4; through *Jour. Amer. Med. Assoc.*, Aug. 21, 1920.)

NEWS ITEMS AND PERSONAL NOTES.

OFFICERS ELECT OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.—The tellers report, that as a result of the mail vote, the following officers of the American Pharmaceutical Association have been elected for year 1921–1922:

President, Samuel L. Hilton, Washington, D. C.

First Vice-President, Charles E. Caspari, St. Louis, Mo.

Second Vice-President, David F. Jones, Watertown, S. D.

Third Vice-President, Hugo H. Schaefer, New York, N. Y.

Members of the Council for three years, Henry M. Whelpley, St. Louis, Mo.; George M. Beringer, Camden, N. J.; John G. Godding, Boston, Mass.

Also that the proposition submitted to a referendum vote, to raise the annual dues from $5.00 to $7.50 and to continue the publication of both the *Journal of the American Pharmaceutical Association* and the *Year Book* was carried by a substantial majority.

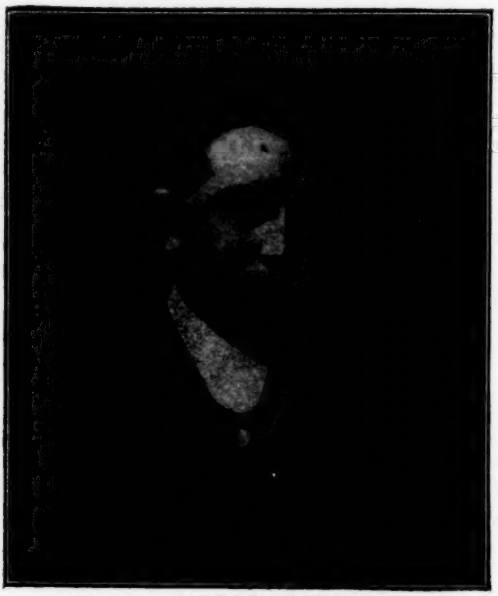
THE AMERICAN DRUG MANUFACTURERS' ASSOCIATION, ANNUAL MEETING AND NEW PRESIDENT.—The next annual meeting of the American Drug Manufacturers' Association will be held in New York City, April 11–14, 1921. The headquarters hotel will be announced later.

Mr. W. A. Sailer, of Sharp & Dohme, has been elected as President for the unexpired term of the late President R. C. Stofer.

NEWLY ELECTED HEAD OF THE NORWICH PHARMACAL COMPANY.

Mr. W. G. Peckham, Second Vice-President and General Sales Director of the Norwich Pharmacal Company has been elected President of that corporation, filling the vacancy caused by the decease of R. C. Stofer.

Mr. Peckham received his early pharmaceutical training in the organization of which he is now the head, having been engaged when sixteen years of age as errand boy in the tablet department.



W. G. PECKHAM.

After six years' experience in which he became an expert tablet man, he accepted a position as foreman of the tablet department of the Geo. L. Claflin Company—wholesale druggists of Providence, R. I., who conducted a manufacturing laboratory in connection with their wholesale business. A year later, at the formation of the Daggett and Miller Company, he became Superintendent of their laboratory and later on, Vice-President and General Manager.

About ten years ago he returned to his first employers as Assistant

Manager of their Chicago branch. A year later, he was made manager which position he has since occupied up to his election as President. In this position he demonstrated exceptional ability and under his régime the business has trebled.

Mr. Peckham is a young man—under forty-five—but his broad knowledge, energy and years of experience in handling the affairs of the Company's largest branch have well fitted him for the presidency of this prominent pharmaceutical industry.

BOOK REVIEWS.

MARGARINE. By William Clayton, M.Sc. Longmans, Green & Co., London. 187 pages, cloth bound. Price, $4.75.

The series of monographs on Industrial Chemistry, edited by Sir Edward Thorpe, has been added to by the publication of this excellent work on Margarine, the first of its kind in any language according to the author.

The work includes a consideration of Oils and Fats Used in Margarine Manufacture, Edible Hydrogenated Oils, Milk Examination, Margarine Manufacture, Theory of Emulsification, Butter and Renovated Butter, Analysis of Butter and Margarine, Deterioration of Butter and Margarine in Storage, Nutritional Chemistry of Fats and Oils.

The book is illustrated with many half-tone plates and figures in the text and contains a complete bibliography of the subject occupying thirty-five pages in the appendix. There are three separate indexes, one for authors, one for patents (American, English and German), and a very complete subject index.

The book as a whole is of particular interest only to the food chemist or food law enforcement officer, but the chapter on the theory of emulsification, which is very complete and up-to-date, makes the book a worth while addition to any scientific library.

C. H. LAW.

THE DETERMINATION OF HYDROGEN IONS. By W. Mansfield Clark, M.A., Ph.D., Chemist, Research Laboratories of the Dairy Division, United States Department of Agriculture. 8vo., 309 pages and index. Williams and Wilkins, Baltimore. $5.00.

The theory of ionization was set forth by Arrhenius in the first volume of the *Zeitschrift fuer physikalische Chemie*, in 1887. As

with all other notable theories or principles in science, foreshadowings of some features of it can be found in the works of earlier scientists, but it is not the one who first "thinks of" anything, but the one who "thinks it out" or establishes it that deserves the greater honor. Dr. Clark informs us in his preface that Pasteur had a distinct perception of the importance of the degree of acidity, although, of course, he did not formulate this in the terms of dissociation or ion concentration. Pasteur pointed out, in his *Studies on Fermentation*, that the relatively high acidity of must favors a natural alcoholic fermentation, while the low relative acidity of wort introduces difficulties in the brewing of malt liquors. There is here probably a theme for an interesting and useful disquisition on the influence of hydrogen ion concentration on the progress of civilization. One writer has declared that the limits of the Roman Empire in northwestern Europe were, in a measure at least, determined by the food and beverage habits of the races. The Romans and their principal auxiliaries were accustomed to wine and olive oil; the tribes of Baltic region used beer and butter. We have good reason to believe that butter is more nutritious than the vegetable oils. The materialistic conception of history has been a prominent theme in later days; is it possible that the world's progress and the solution of the problem of the league of nations will be reduced finally to an equation involving log. p_H?

We are dealing, however, with a work of special type and of novel purpose. Chemists have, at last, the important and difficult problems of hydrogen ion concentration presented in extended and careful manner and explained in detail. Dr. Clark points out that of all the secondary inferences drawn from the general theory of ionization, the most important is that relating to the resolution of "acidity" into two components—the concentration of hydrogen ions and the quantity of acid capable of furnishing those ions. For two reasons the concentration of the hydrogen ion occupies a unique place in the phenomena of ionization. The factor of concentration is now known to be of very great importance in biologic chemistry. Already, many data have been collected as to the extent which the soil acids are ionized, and in this connection, it must be noted that the older methods which merely determined the total acidity by titration, for instance, with alkali, do not give the real reaction of the soil solution to the living tissues with which they are in contact. It is a question, indeed, whether, in the light of the development of

this phase of the subject, a large part of the earlier data of soil analysis may not have to be scrapped. Another point about hydrogen ion concentration is that at present the determination of it is among the most satisfactory of ordinary laboratory processes. Of course, as Clark points out, there is danger of making the subject a fetish, by which undue weight may be given to a secondary phase of a problem, or a generalization much wider than is justified be made. There is always a tendency to make too much of the new view.

A commendable feature of the book, although it may seem, at first, merely minor detail, is the symbol used for the factor of concentration. Sörensen, to whom is due so much of the development of the matter, introduced a symbol somewhat complicated in typographic form, and hence some difference is noted in the manner in which it is written and printed by different authorities. Leeds and Northrup, in a recent publication, use the original Sörensen form, but Clark uses the simpler form, P_H. This, also used by the *Journal of Biological Chemistry*, is much more easy for the compositor and fully as satisfactory to the chemist. There seems to be no reason for retaining a complex expression merely because it is the form originally suggested.

The procedures given in the book are wisely limited to the two types by which the concentration determinations are made in the working laboratory, that by indicators and that by electrometric methods. Both these methods are described in great detail. The theory of indicators has been the subject of extensive study among chemists, and the phenomena of color change under the differences of acidity and alkalinity are striking even to the experienced worker. The chemical and physical changes occurring in many indicators are complicated, involving even the reactions of tautomerism. Advance in the practical application of these substances has, however, brought out the fact that by the use of what are termed "buffer" solutions, indicators may be classed empirically, *i. e.*, without taking into consideration any theory. These buffer solutions are standard solutions of such well defined composition and hydrogen ion concentration that they can be accurately duplicated. For the highest accuracy, the degree of ion concentration should be verified by the electrometric method, which is an absolute one. They generally consist of a mixture of some acid and one of its alkali salts, Clark and Lubs have designed a set of these, the details of which

are given in the book. A double page color plate gives the range of tints resulting from different degrees of hydrogen ion concentration in action with a series of indicators of comparatively recent introduction and special adaptability to the problem in hand.

The book will be a great aid to the working chemist and especially to the bio-chemist. It is well printed, on good paper with good type and the literary merit is high, the language being clear and concise. An extensive bibliography and an account of many of the applications of the principle are added.

The book bears the statement "Published by the permission of the Secretary of Agriculture." Well, we suppose it is all right. Dr. Clark is a subordinate of that official, and presumably his work belongs to the government, and it is likely that the "permission" is mere routine, yet it does give the independent chemist a twinge to see the publication of such meritorious work even nominally dependent on an official who may not know anything about the matter.

HENRY LEFFMANN.

"A CRITICAL REVISION OF THE GENUS EUCALYPTUS." By J. H. Maiden, I.S.O., F.R.S., F.L.S., Government Botanist of New South Wales and Director of the Botanic Gardens, Sydney. Vol. V, Part 2.

This constitutes part XLII of the complete work, which we have reviewed from time to time as the parts have been received. The present contribution to this monographic study of the interesting Genus Eucalyptus covers the following species: *E. eximia Schauer; E. peltata Bentham; E. Watsoniana F. v. M.; E. trachyphloia F. v. M.; E. hybrida Maiden; E. Kruseana F. v. M.; E. Dawsoni; R. T. Baker; E. polyanthemos Schauer; E. conica Deane and Maiden; E. concolor Schauer.*

The same style of description and excellence of illustrations that characterize the former parts of this voluminous study are exhibited in the part now before us.

G. M. B.